BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 8 1949

CLINICAL AND SOCIAL PROBLEMS OF EPILEPSY*

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LECTURE II

The Causes of Epilepsy

There are two ways of looking at the problem of epilepsy in an aetiological sense. One is to regard all forms of convulsive attack as epilepsy, which then becomes simply a symptom of many general and nervous diseases: Cobb (1936) lists sixty clinical causes of fits. The other is to reserve the term for an essentially neurogenic disorder in which there is episodic disturbance of cortical function: this would include idiopathic epilepsy, and might reasonably include also symptomatic epilepsy due to primary intracranial disease. It would exclude convulsions due to general circulatory changes, to circulating toxins, or to metabolic poisons. According to this definition it would be correct to speak of cysticercosis epilepsy or traumatic epilepsy, but incorrect to speak of "cardiac epilepsy," "hypoglycaemic epilepsy," or "uraemic epilepsy." This clinical classification seems to me a useful one.

In every case in which an initial diagnosis of epilepsy has been made two further aims should be in the mind of the physician: (1) to determine the part of the brain in which the disturbance starts; (2) to decide the nature of the lesion at that point.

The Anatomical Diagnosis.—Localization of the site of the discharge is clinically precise in local epilepsy of all types and in generalized seizures with consistent focal onset. Lennox and Cobb (1933) instituted an inquiry into the aura or first stage of the fit in 1,359 patients. A similar inquiry was made by Gowers (1901) in 2,013 patients, and it is remarkable to find that the percentage reporting an aura of some kind is almost identical in the two series—namely, 56.2% and 57%. An aura occurred with equal frequency in idiopathic and symptomatic cases, but in only a minority was it of precise localizing significance. Aid in localization is also given by electro-encephalography, and Jasper (Penfield and Erickson, 1941) believes that such records have their chief value in demonstrating or confirming the focal origin of attacks.

The Pathological Diagnosis.—Determination of the site of a discharging lesion or epileptogenic focus, if this is possible, does not of itself, as Hughlings Jackson pointed out, give any information about the nature of the lesion An initial approach to the problem of the pathological diagnosis is afforded by consideration of the types of cerebral lesion which predominate at different periods of life. Thus in infancy the chief organic cerebral causes of epilepsy are developmental brain defect and birth injury. Such injury may result from prolonged asphyxia or from cortical laceration, and in these children there are generally other evidences besides epilepsy of diffuse or focal brain injury. It is important to remember that the development of fits originating from the neighbourhood of the injury may be delayed until later childhood or even adult life (Penfield and Erickson, 1941). Acquired cerebral lesions of childhood are often followed by epilepsy. In these, as in birth trauma, there are likely to be focal signs of brain injury, especially hemiplegia. Occurring as a complication of infections of known and unknown nature, and accompanied at the outset by convulsions, the cerebral injury is probably more often due to vascular thrombosis than to encephalitis. After childhood the major organic cerebral causes of epilepsy are head injury, cerebral tumours, and cerebral arteriosclerosis. These have their maximum incidence in early adult life, middle age, and old age respectively.

Significance of Infantile Convulsions

Assessment of the significance of convulsions in an individual child is a clinical problem involving a weighing of the evidence. The presence of signs of pre-existing brain defect or injury is unfavourable. Recurrent attacks occurring at intervals without known exciting cause are strongly suggestive of idiopathic epilepsy, which is likely to continue. Petit mal attacks have the same significance. These considerations apart, an isolated convulsion or a short series of convulsions occurring in early childhood during an acute infective illness, and unaccompanied by persisting evidence of brain damage, need not cause anxiety about the future or call for continued anticonvulsant treatment: the great majority of such children do not develop epilepsy. This is in accordance with the usual belief, but does not justify a tendency to regard infantile convulsions generally as of little moment.

Age of Onset of Idiopathic Epilepsy

A diagnosis of idiopathic epilepsy implies the exclusion so far as is possible of all organic cerebral lesions and in general a tendency to recurrence of attacks without known cause. Idiopathic epilepsy may arise at any age, but does so especially in childhood and youth. An onset in later years is usually stated to be decidedly infrequent. Most textbooks contain warnings such as the following: "It is always well to be suspicious of 'epilepsy' beginning in adult life, for in a majority of such cases the disease is not epilepsy" (Christian, 1942).

Organic disease of the brain which may cause epilepsy is commoner in later life, and therefore epilepsy in such patients is more likely to be due to progressive intracranial disease than in children or adolescents. Nevertheless I see many patients whose fits begin in adult life and continue

*The second Lumleian Lecture, delivered to the Royal College of Physicians, April 15, 1948 (abridged). Lecture I appeared in last week's issue.

without evidence of any structural basis for the attacks. In order to clarify this matter I have made an inquiry into the age of onset in my cases, and secondly into the cause of attacks in the later age groups.

Table I shows the age of onset in 991 cases. While, in accordance with general experience, the highest incidence is in the second decade, it will be noted that 12% showed the first evidence of epilepsy between the ages of 30 and 40 and 17% after the age of 40.

TABLE I.—*Age of Onset of Epilepsy in 991 Cases*

0–10 years	19%	31–40 years	12%
11–20 „	30½	Over 40 „	17%
21–30 „	22%		

Table II shows a comparison of this series with some previous records.

TABLE II.—*Percentage of Cases of Epilepsy with Onset over Age 30*

Gowers	Turner	Spratling	Starr	Kraepelin	Paskind	Present Series
9·3	9·8	7·4	12·7	12·8	19·2	29·0

It will be noted that the figures of Paskind (1932) and my own series indicate a markedly higher proportion than the others of patients in whom the first fits occurred after the age of 30. This observer's statistics and my own are comparable because we were both dealing with patients in private practice or in the purely consultative out-patient service of a general hospital. Most if not all of the other assessments were made on patients in institutions or attending special hospitals for epilepsy. These represent a more severe and deteriorated group, and in such patients the age of onset is earlier. Of Paskind's patients 93.5% were in excellent mental health and were engaged in occupations similar to those of the great mass of the population. Tylor Fox (1939) states that there are about 20,000 epileptics in various institutions in this country, and estimates that there are at least 100,000 in the community at large. The extramural group is therefore more representative of epileptic patients as a whole.

Table III gives the results of a follow-up, after not less than three years, of 100 cases of epilepsy with onset after the age of 40.

TABLE III.—*Follow-up of 100 Cases of Epilepsy with Onset after the Age of 40*

Deaths		25
Tumour—proved 8, probable 2	10	
Effects of cerebral arteriosclerosis	5	
Heart failure	3	
Air raid	1	
Pancreatic tumour ? hypoglycaemia	1	
G.P.I.	1	
Cause unknown	4	
Improved (fits ceased or diminished)		48
I.S.Q. or worse		27

Of the 25 deaths 10 were due to intracranial tumour and five to cerebral arteriosclerosis. Of the 75 surviving patients none showed on re-examination any symptom or sign of intracranial tumour. Their general condition on the whole was good: most of them were living almost normal lives and were at work. A gratifying number seem to have been much improved by treatment.

Evidences of arterial disease are not conspicuous in these patients. Without doubt cerebral arteriosclerosis may cause epilepsy. But it is not justifiable to assign seizures to this cause merely because the patient is of advanced age. Analysis of blood pressure readings does not seem to indicate the presence of hypertension in these epileptic patients in any greater proportion than in non-epileptic subjects of the same age.

Other evidences of cerebral arteriosclerosis—for example, strokes and mental deterioration—were notably infrequent.

The question arises whether Jacksonian epilepsy is specially suggestive of tumour. Of the 100 patients with onset after the age of 40, 11 are known to have had Jacksonian attacks (Table IV). Of these 8 are dead, the cause being shown.

TABLE IV.—*Significance of Jacksonian Epilepsy among 100 Patients*

Number known to have Jacksonian attacks	11
Deaths	8
Tumour	3
Cerebral arteriosclerosis	1
G.P.I.	1
Heart failure	2
Unknown	1

The mortality is unexpected, but the point which emerges is that Jacksonian attacks, while revealing the site of the disturbance, give no indication of the nature of the lesion.

One further point of clinical significance is the time of attacks. For the 75 surviving patients this is shown in Table V.

TABLE V.—*Time of Epileptic Attacks in 75 Patients over Age 40*

Diurnal only	31	Irregular	17
Nocturnal only	27		

A final statistical item invites an approach from another angle—namely, the incidence of epilepsy in a series of intracranial tumours. My colleague G. F. Rowbotham has kindly allowed me to analyse the records of 200 consecutive cases of verified tumour admitted to his clinic in the course of about two years.

TABLE VI

Incidence of Epilepsy in 200 Cases of Intracranial Tumour

Number with fits	56 (28%)
Number with fits at onset	38 (19%)
Grand mal	22
Jacksonian	14
Petit mal	2

Time of Appearance of other Signs of Tumour in 38 Cases with Epilepsy at Onset

Period	No. of Cases	Period	No. of Cases
1– 6 months	10	5– 6 years	1
6–12 „	8	6– 7 „	2
1 –2 years	5	7– 8 „	1
2– 3 „	4	8–10 „	1
3– 5 „	5	10–12 „	1

Fits occurred in 28% at some stage. In 19% the patients came under observation because of some type of epileptic attack. In more than half the initial attack was of the grand mal type, in about a third Jacksonian; while in two patients the earliest attacks were of the petit mal variety. Half of these patients with epilepsy at the onset developed other symptoms and signs of intracranial tumour within twelve months. In the remainder such evidence was delayed up to five years, and in isolated cases up to twelve years.

Glioma of a cerebral hemisphere was much the commonest cause of fits; cases which were latent for several years were either astrocytomas or meningiomas. High intracranial pressure *per se* is not an important cause of fits; for example, they are rare in posterior fossa tumours, though these are usually associated with early internal hydrocephalus.

Similar conclusions have been published by a number of observers (Sargent, 1921; Parker, 1930; Dowman and Smith, 1928; Penfield and Erickson, 1941), though the time relationship between epilepsy and other symptoms has not to my mind been sufficiently stressed. The proportion of cases with epilepsy at the onset is considerably lower in most of these reports.

Discussing the causes of epilepsy, Penfield and Erickson (1941), while recognizing that idiopathic seizures may start

at any time, write as follows: "In cases of onset between 35 and 55, the most frequent cause is cerebral neoplasm." "After 55 years the various cerebral lesions produced by abnormality of the cerebral blood vessels become more frequent, though the strong probability of neoplasm must still be remembered." "Idiopathic epilepsy comes on in youth, not in early infancy, and not in middle age or old age."

With reference to these conclusions I would point out that statistics about epilepsy are affected by the tendency for the patients to fall into different groups. There is the broad division between institutional and non-institutional cases. There is also, I think, a process of selection operating in regard to patients sent to neurological surgeons: in a personal communication Penfield agrees with this opinion. I would be the last to minimize the importance of seeking an organic cause in all cases, and especially in patients of tumour-bearing age, but I cannot avoid the conclusion that among epileptics as a whole the largest group must still be classified as idiopathic. When fits are due to tumour careful observation reveals other symptoms and signs within a few months in the majority of cases if these are not already present at the onset of the illness.

Aetiology of Idiopathic Epilepsy

The term "idiopathic" is a deliberate declaration of aetiological ignorance. Without doubt a proportion of cases so classified are due to unrevealed structural causes. Of the remainder it seems probable that the chief cause is an inherited instability of the cortex. But if this is so, then what is inherited is infrequently actual epilepsy; more often a less specific dysrhythmia.

Evidence about heredity is derived primarily from studies of family histories. It has been estimated that 1 in 200 to 300 of the population as a whole has had fits at some time. Among the near relatives of epileptics 1 in 40 to 50 has had fits (Lennox, 1945b). That is to say, seizures are five to six times more frequent in the parents, siblings, and children of epileptics than in the general population. Taking relatives as a whole and not only near relatives, a family history of epilepsy has been obtained by various observers in some 4% of non-epileptics and in from 20 to 30% of epileptics. This figure is less when attacks begin in adult life. Very striking is the finding in a series of identical twins that in 70% of these if epilepsy was present in one twin it was present in the other (Lennox, Gibbs, and Gibbs, 1940).

Further evidence comes from electro-encephalographic records. Soon after the initial discovery of distinctive records in epileptic attacks several observers (Lowenbach, 1939; Strauss *et al.*, 1939) recorded abnormal waves in the relatives of patients. In one study 60% of the near relatives of a group of epileptics were found to have various abnormal rhythms, as compared with 10% of controls with no such family history (Lennox, Gibbs, and Gibbs, 1940). It is important to note, however, that the proportion of relatives whose records showed paroxysmal disturbances of specifically epileptic type was much smaller. Again of special interest is the observation (Lennox, Gibbs, and Gibbs, 1942) of seven pairs of identical twins: one of each pair had epilepsy, and in each instance the other twin showed a significantly abnormal record.

These studies of family trees and electro-encephalograms agree in showing a hereditary predisposition which is very much more frequent than the direct inheritance of epilepsy. It has been suggested that epilepsy results when acquired factors such as trauma or tumour combine with genetic factors. This theory is attractive, but seems to have only a limited application, since in the majority of cases no exciting cause can be found for the onset of overt epilepsy.

Medicinal Treatment

On May 11, 1857 (vide *Lancet* of that date), Sir John Locock presided at a meeting of the Royal Medical and Chirurgical Society of London at which an address on epilepsy was given by Sieveking. In the discussion Locock mentioned that he had been trying treatment by bromide of potassium at the suggestion of an unnamed German physician. The suggestion was made because this medicine had been found to depress sexual activity, and the idea had long been prevalent that masturbation was an important cause of epilepsy. This belief persisted: as late as 1880 a paper was read at the annual meeting of the British Medical Association at Cambridge on the treatment of epilepsy by castration (Temkin, 1945). Bromides in various combinations became the first effective treatment of this disease, and remained unchallenged for fifty years.

Phenobarbitone

Medicinal treatment is now more hopeful than in the past, but rather more complex because several drugs of proved efficacy are available and it is necessary in each case to decide which remedy or combination of remedies is most likely to be successful. Phenobarbitone has very largely replaced bromides because both clinically and experimentally it is a more effective anticonvulsant, is easier to take in tablet form, and is almost free from toxic effects. The dose which can be tolerated without drowsiness varies very much in different individuals. It is generally sufficient to give it morning and night in a dose of 1½ gr. (0.1 g.) for an adult, but this may be pushed considerably higher in some patients if control of attacks is inadequate. Patients who have only nocturnal attacks may take a rather larger dose at night, but it is probably best not to omit altogether a smaller morning dose, because if it is given only once in twenty-four hours there is a tendency for attacks to be postponed to the uncontrolled period. When the optimum dose has been decided it should be maintained with great regularity: if attacks have been absent for three years it may be reduced gradually and finally discontinued. Sudden cessation frequently leads to return of attacks.

"Epanutin"

In an exhaustive series of experiments Merritt and Putnam (1945) found that the most effective anticonvulsant tested was the sodium salt of 5, 5, diphenyl-hydantoin, known in this country under the approved name of soluble phenytoin and "epanutin," and as dilantin sodium in America. A large number of reports have been published since this drug was introduced ten years ago (Parke, Davis and Co., 1945). There is no doubt it is the most powerful anticonvulsant known, and it has the great advantage that in therapeutic doses it has practically no hypnotic effect. It is especially potent in the control of psychomotor attacks. It has not, however, displaced phenobarbitone, because with its use there is a much higher incidence of toxic effects. These are rarely dangerous, but they may be alarming, and the margin between the effective therapeutic dose and the toxic dose is often narrow.

When toxic symptoms occur they usually do so early in treatment, but occasionally they appear after several months. Nausea and vomiting are generally avoided by giving the remedy with meals. Erythematous rashes with fever are infrequent but necessitate withdrawal of the drug, with resumption in gradually increasing doses. The most frequent and disturbing effects are referable to the nervous system, and include nystagmus and diplopia, tremors, and ataxia of upper and lower limbs.

A curious oedema of the gums has been reported with varying frequency in different series. In spite of much work on it the nature of the change is obscure: its incidence is diminished by preliminary removal of oral sepsis, and continued care of the teeth and massage of the gums usually render it unnecessary to discontinue the drug.

No serious blood changes have been reported from the use of epanutin.

The usual minimal effective dose for adults is three capsules (each 1½ gr.: 0.1 g.) daily, one with each of the principal meals.

If a distinct effect is not observed a fourth dose may be added, and further additions may be made in cases under continuous observation. Most British reports on this remedy come from institutions, and therefore concern severe cases and usually those which have failed to respond satisfactorily to phenobarbitone. For less severe cases it is not always necessary to give full doses; furthermore, if the treatment is begun and increased gradually toxic effects are lessened (Pullar-Strecker, 1945).

Both phenobarbitone and epanutin are anticonvulsants and of chief value in the control of major seizures. They are often without effect on petit mal, and indeed epanutin may increase the number of attacks of this type. In cases resistant to either drug alone a combination of the two may prove more effective. Such combined medication is in fact very commonly used, but it is important to realize that if this plan is followed the dosage of each drug should be adequate. There is reason to believe that the action of the two is different: the beneficial effects of the second drug are not obtained unless it is given in sufficient amount to produce an effect by itself, and the toxicity of the one is neither enhanced nor diminished by the other (Blair, 1947).

"Tridione"

The frequent failure of the anticonvulsants to influence petit mal gives importance to the introduction of a drug which has a striking effect on this type of attack and also on the allied akinetic seizures and on epileptic myoclonus. This is 3,5,5-trimethyloxazolidine-2,4-dione, or "tridione," and its use for epilepsy is due to Lennox. It has become available in this country only in the past few months, and only one report has yet been published by a British observer (Butter, 1948). I can therefore only speak of it from a very limited personal experience, but it may be useful to mention the main facts as set out in the careful reports from America, where some 10,000 patients are being treated with it. Lennox (1945a, 1947) reported that of 166 patients 31% had been entirely freed of attacks, and in 32% attacks were less than a quarter of their previous number; 83% in all had fewer seizures. Furthermore, in many cases the distinctive paroxysmal spike-and-wave pattern of the electro-encephalogram was restored to normal. He emphasizes that the drug is wrongly described as an anticonvulsant, for not only is it ineffective against convulsive seizures but it may increase these if they already exist.

This remedy is given in capsules of 0.3 g., and the usual dose is three capsules a day for children over 5 years, and four capsules a day for adults, taken with meals. For small children the contents of a capsule may be given with food. The effect on attacks may be immediate, but the maximum effect is usually seen in one to four weeks; the longest period of waiting for relief was six months.

Toxic effects were soon noted. About one in seven patients develops a rash, either a papular rash on the forehead or a morbilliform eruption; if the latter is generalized it is advised that the drug be stopped for a few days and resumed gradually. About one-third of the patients complain of intolerance of bright light; the degree of this symptom, the nature of which is unknown, varies, and it seldom necessitates stoppage of the remedy. No evidence of injury to the retina or optic nerves has been detected. Such toxic effects are rarely serious, but in 1946 two reports (Harrison *et al.*, 1946; Mackay and Gottstein, 1946) were published simultaneously of fatal aplastic anaemia and agranulocytosis due to this drug. It had been given for six months and ten months respectively, when the blood changes appeared suddenly and could not be controlled by any measures. Including these two, Lennox has learnt of four fatal cases. Two further cases have been reported in this country. One (Braithwaite, 1948) had a transient urticarial rash on the 25th day; on the 51st he developed gingivitis and pyrexia. The drug was stopped on the 53rd day, but he died three weeks later with agranulocytosis and an aplastic marrow. The second died, after four weeks' treatment, from exfoliative dermatitis without any blood changes (Kerrin, 1948). These fatalities may reasonably be attributed to idiosyncrasy, and are perhaps no more frequent than with some other drugs, but such drugs are seldom administered for long periods, while remedies for epilepsy have usually to be continued indefinitely. It is therefore important to learn that withdrawal of tridione, unlike phenobarbitone and epanutin, is not followed by an early return of attacks, and in many cases they have not returned at all. Lennox advises that if attacks have been absent for three months the drug should be reduced gradually and finally discontinued. He believes that if monthly blood examinations are done danger can be averted by stopping the drug if the polymorph count falls below 1,600 per c.mm. In 127 patients who had taken tridione for periods up to two years he found that the count fell to this level in 6%, in all cases returning to normal when the drug was stopped. My own experience, though limited to 9 cases, is favourable: in all attacks have been reduced and toxic effects absent except for some complaint of the glare phenomenon. The leucocyte count has not fallen in any case, but tended to rise. In three of these patients attacks have now been absent for three months and the drug is being withdrawn.

Summary of Medicinal Treatment

It may be said that, if a patient suffers from grand mal only, the choice lies between epanutin and phenobarbitone. In young subjects, in whom it is desirable to bring the attacks under control as quickly and certainly as possible because of the danger of mental deterioration, the more powerful remedy epanutin should in my opinion be used provided the necessary observation can be maintained. Alternatively, phenobarbitone may be used in the first instance. If after due observation attacks are not controlled, epanutin should be added gradually without reducing the dose of phenobarbitone. In such cases it is probably best to continue the two drugs together, but reduction in the amount of phenobarbitone may be tried.

When the patient has both grand mal and petit mal control of the former is the more important, but if attacks of the latter are frequent tridione should be used as well as an anticonvulsant. In this event phenobarbitone should be chosen, since epanutin tends to increase petit mal.

For psychomotor attacks epanutin is much the most effective agent. For pure petit mal the evidence I have indicated points to the use of tridione with the appropriate precautions.

Status epilepticus calls for urgent control by full doses of sedative. Probably the safest and most effective method is the intramuscular injection of 5 to 10 ml. of paraldehyde, repeated if necessary. Alternatively, soluble phenobarbitone may be injected in 3-gr. (0.2 g.) doses.

Finally, in this connexion I would quote the words of Blair (1940), that with the remedies now available there are few epileptics who cannot expect reasonable control of their fits, and hope should never be abandoned until these treatments have each been patiently and efficiently tried out.

Surgical Treatment

Epilepsy *per se* is not an indication for surgical intervention. If it can be shown that attacks are arising from a local brain lesion, operation may be justified in the hope of removing the epileptogenic focus. If this is a tumour, relief of fits is only an incidental aim of operation. Non-progressive lesions may be manifested solely by epilepsy; such lesions are meningocerebral scars resulting from traumatic, vascular, or inflammatory changes. Their presence may be suspected because of local epilepsy or generalized epilepsy with consistent focal onset, together with indications from the history of the manner in which they might have originated. Any persistent evidence of impaired function, such as minimal signs of hemiplegia, would of course be decisive evidence of a local lesion. But attacks of both these types occur commonly in idiopathic epilepsy, and a negative exploration may make the patient worse. In these circumstances radiographs after the introduction of air by lumbar puncture provide evidence of the greatest importance (Childe and Penfield, 1944). To this method may now be added the demonstration of a focal lesion by the electro-encephalogram.

Decision about operation if a local lesion has been demonstrated is by no means simple. It has to be remembered that epileptic attacks do not arise directly from an area of cortical fibrosis but are the result of instability produced by the scar in neighbouring but intact cortical cells. Therefore attacks may continue in spite of a clean excision, and anticonvulsant treatment must be maintained. Excision of such an area means replacing one scar by another and possibly converting a discharging lesion into a destroying lesion. In each case the frequency of attacks, the effects of a full trial of medicinal treatment, and the risks of injury by the operation have to be taken into account.

Social Problems of Epilepsy

The social consequences of epilepsy are peculiarly severe, and it is our duty to mitigate them so far as lies in our power. Nothing can alter the fact that a liability to sudden and unpredictable attacks of loss of consciousness or of uncontrolled behaviour is a grave handicap to any human being. In this respect epilepsy is much more serious than any other of the paroxysmal disorders, and this is a reason for a separateness and not a unity of these disorders.

Two fears fill the minds of the parents of a child with epilepsy—the fear of accident and the fear of mental deterioration. That dreadful accidents can occur we all know, but when we consider the immense aggregate of fits which occur among epileptics in the community we must recognize that serious accidents from this cause are relatively very few. The danger of mental deterioration when attacks begin in childhood is real enough, but is usually much exaggerated in the parents' thoughts. Though there are exceptions, this danger is on the whole proportionate to the frequency and severity of attacks: the risk is therefore diminished by the improved methods of treatment now available. Children with pure petit mal, and the great majority with only occasional grand mal, are in little danger of mental change. Presentation of these facts is of incalculable value to the parents, and is to be preferred to vague promises and hopes.

The first serious social decisions are concerned with education. Frequent major seizures are incompatible with ordinary school life. Petit mal attacks, even if numerous, are almost devoid of risk and should not prevent attendance at school. Infrequent major seizures should not be a barrier. The welfare of the children as a whole must be the first consideration, but if the attitude of teachers is free of fuss and anxiety the witnessing of an occasional attack by other children does these children no harm. Few if any of the school activities should be denied to the epileptic boy or girl. To exclude games for fear of head injury is to provoke greater risks to the child's physical development and peace of mind. Swimming is more doubtful, and must be under supervision ; but each case must be considered on its merits, frequency and time of attacks being all-important. To prohibit cycling may cause much unhappiness and is by no means always necessary. Examinations should be taken in the ordinary way. Nothing must prevent the regular supervision of medicinal treatment.

Interesting studies have been made of University students subject to epilepsy. In one such study of 93 students (Himler and Raphael, 1944) 76% were classified as of the idiopathic group ; the rest had some evidence of cerebral injury or defect: 65% to 70% did creditable work and took up jobs of all kinds, including medicine. Of 70 epileptic students at another University (Lennox, 1946) the number graduating equalled the record for all students.

Such facts have a bearing on the important question of choice of occupation. Essentially a decision depends on the degree to which attacks are controlled by treatment. Short of complete control, however, infrequent attacks should seldom be held to prevent a young man from adopting the occupation of his choice. Certain callings are clearly unsuitable. They include contact with dangerous machinery, work at heights or in the mines, or any post in which an attack might involve danger to others. It is not in our discretion to give permission for a patient subject to epilepsy to drive a motor vehicle, for this is his own responsibility. The law, being unsatisfactory (Symonds, 1948), is in fact widely evaded.

Medicine, law, the arts, and many office occupations need not be regarded as closed, for there are branches of these which can be pursued with success and safety, though others are barred. For those with no special ambitions more specific advice may be given, and I have been accustomed to suggest work on the land, which is healthy, active, and satisfying, and involves little restriction apart from possible avoidance of agricultural machinery.

As a fact the great majority of adult epileptics outside institutions earn their living in every variety of calling, and many have achieved fame in every walk of life. These people form by far the largest group of all sufferers from epilepsy. They are a relatively stable group and do not deteriorate as the years pass, but rather tend to improve. The more serious cases beginning in childhood have been weeded out. But though they are at work for the most part, they suffer serious social disabilities. Many conceal their liability to fits and go in fear of an attack at work which will lead to loss of their employment.

Hitherto probably the greatest deterrent to the securing of work has been the liability of employers for accidents arising out of and in the course of employment. Replacement of the Workmen's Compensation Act by the National Insurance (Industrial Injuries) Act should greatly assist in the employment of epileptics in common with other partially disabled persons. The need for full use of man-power, as well as an increased sense of social responsibility, led to the Disabled Persons (Employment) Act of 1944, under the provisions of which a proportion of disabled persons must be accepted by all employers of more than twenty people. The Act provides for registration as a means of identifying those who are qualified for its benefits, and responsibility for finding suitable employment is in the hands of Disablement Resettlement Officers (D.R.O.s) working at the Employment Exchanges. For those judged unfit for ordinary employment, work may be found in sheltered workshops maintained under the Act by the Disabled Persons' Employment Corporation: eight of these factories have been established throughout the country and fifty more are planned. Special provision for epileptics has been made in certain of these factories.

Apart from official help, voluntary organizations, including the hospital almoners' service, are ready to assist epileptics to get and keep jobs, and are endeavouring to overcome prejudice and ignorance on the part of employers and the public in regard to this disease. In this country Tylor Fox (1939, 1947), and in America Lennox (Lennox and Cobb, 1942), have in particular been tireless in their efforts to improve the lot of epileptics in the community. The success of all plans depends entirely on the initiative and co-operation of those in medical charge of the patients. We alone know when it is reasonable to ask employers to accept such persons in their factories or offices ; school and University authorities look to us for guidance in the difficult decision whether to accept a student or pupil known to be liable to fits. To recommend unsuitable patients is to do harm to them and to epileptics as a whole. No two cases are exactly alike ; frequency and character of attacks are clearly the main considerations, but favourable points are

the occurrence of attacks chiefly or solely during sleep or in the early mornings, the existence of a warning long enough to enable the patient to avoid heavy falls, and a satisfactory degree of control by medicinal treatment.

One further social problem is that of marriage. On the basis of the evidence about the heredity of epilepsy formerly noted, the chance of a child of an epileptic also becoming epileptic has been variously estimated as from 1 in 10 to 1 in 40 (Brain, 1926; Lennox, 1945b). The risk of transmission is probably much less still if attacks begin in adult life, or if the patient has no family history of epilepsy; also if attacks are the result of a definite brain injury. A family history in both partners greatly increases the risk. Electrical records of epileptic type in either partner or both partners have probably the same significance. The prospect of producing epileptic children is therefore far less than is generally believed, and this we can conscientiously explain to those concerned. The real risks in marriage are the anxieties and dangers caused in the home and at work by the attacks themselves: these known risks can be calculated and faced. Nevertheless, so great is the dread of epilepsy that many patients decline marriage or refuse to have children. Both decisions are probably wrong, but they are understandable.

I have pleasure in acknowledging the help of successive assistants in following up cases—namely, Drs. H. G. Miller, F. Robertson, R. Mowbray, G. C. Ismay, and J. P. Anderson.

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DIABETIC FERTILITY, MATERNAL MORTALITY, AND FOETAL LOSS RATE

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Fertility

Pregnancy in diabetic women in the pre-insulin era was a rare event. Skipper (1933) credits Bennewitz (1826) with the first recorded case. Amenorrhoea due to uncontrolled diabetes accounted for the low fertility rates of 2–6% quoted by Lecorché (1885), von Noorden (1909), and Skipper (1933). The diabetic control that followed the introduction of insulin in 1923 largely abolished the amenorrhoea and produced a concomitant increase in fertility.

Skipper (1933), reviewing the records of the London Hospital, noted a fertility rate of 15% amongst 177 diabetic women between 1923 and 1931, compared with a rate of 2% amongst 190 comparable diabetic women between 1893 and 1922, while Eastman (1946) observed a fertility rate of 28.6%.

The rate of diabetic to non-diabetic pregnancies admitted to large obstetric hospitals has shown a similar rise. Williams (1909) saw only one pregnant diabetic during his thirteen years in charge of the obstetric service at Johns Hopkins Hospital, and in his review of the literature found only 65 recorded cases, whereas Mengert and Laughlin (1939) quote a ratio of 1 in 276, Barns (1941) 1 in 930, and Eastman (1946) 1 in 282. There were 70 diabetic pregnancies among the 20,438 confinements at the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, between 1943

*This work was carried out during the tenure of a Lund Research Fellowship of the Diabetic Association.

and 1947—a ratio of 1 in 292. Insulin has therefore raised the status of the pregnant diabetic from that of a medical curiosity to one for which adequate provision must be made in any maternity service.

Maternal Mortality

An immediate maternal mortality of between 25 and 30% in diabetic women was associated with pregnancy in the pre-insulin era (Duncan, 1882; Offergeld, 1908; Williams, 1909; and others). The last-named author noted an immediate mortality of 27%, with an additional 23% during the ensuing two years, due to diabetic coma in the majority of cases. The insulin era has been associated with a progressively declining maternal mortality. Reviews of the literature by Skipper (1933) and Kramer (1935) revealed immediate maternal mortalities of 9.3 and 3.4% respectively. A mortality rate of less than 2% was quoted by Lawrence and Oakley (1942). White (1946) reported the loss of only one mother in 271 diabetic pregnancies between 1936 and 1946. Several smaller series of cases reported by Kramer (1935), Brandstrup and Okkels (1938), Shir (1939), Mengert and Laughlin (1939), and others reveal no maternal loss. There was one maternal death among the 70 pregnancies in the 62 diabetic women confined at the Simpson Memorial Maternity Pavilion, Edinburgh, between 1942 and 1947. It is thus apparent that the introduction of insulin has made pregnancy relatively safe for diabetic women.

Foetal Loss

The beneficial effects on the mother from insulin treatment have not been shared by the foetus. Henley (1947), reviewing the literature, noted a foetal loss of 43% in 169 pregnancies during the pre-insulin era, compared with 37.6% in 924 pregnancies since the introduction of insulin. The foetal loss rate in his own series was 55%.

The published figures of the foetal loss rate show considerable disparity. Mengert and Laughlin (1939) and Miller, Hurwitz, and Kuder (1944), considering only the foetal deaths occurring late in pregnancy and the deaths of babies during the neonatal period, found the foetal loss rate to be 18.2 and 23.6% respectively. On the other hand the foetal loss rates reported by Ronsheim (1933), Herrick and Tillman (1938), Barns (1941), and Lawrence and Oakley (1942), covering the whole course of pregnancy and the neonatal period, were 64, 43, 44, and 37% respectively.

Throughout this review of our cases the term "foetal loss rate" is taken to mean the percentage of all pregnancies not resulting in the birth of a baby living for at least 14 days. The term is therefore inclusive of all abortions, miscarriages, intrauterine deaths, stillbirths, and deaths occurring during the first 14 days of the neonatal period.

Using this definition, Table I shows that in spite of medical and obstetric supervision which we hope has been at least not inferior to the average in the country our foetal loss rate during the last five years has been as high as 51.4%.

TABLE I.—*Diabetic Foetal Loss Rate*

Period since Diagnosis of Diabetes	Total No. of Pregnancies	Foetal and Neonatal Loss	Foetal Loss Rate
0–2 years	35	19	54·3%
3 years and over ..	35	17	48·6%
Total	70	36	51·4%

In comparison with such figures recent results published by White (1946) are striking. This worker uses hormonal therapy to correct abnormal gonadotrophin and pregnanediol levels. She reports foetal loss rates based on whether these levels are normal or abnormal and on whether patients have been given hormonal treatment of sufficient intensity to correct any abnormality which may exist. She found a foetal loss rate of only 3% when hormonal levels were normal, in comparison with 48% in cases with abnormal levels; but correction of abnormal levels by appropriate therapy resulted in a fall of the foetal loss rate to 10%. Her series, however, does not include abortions before the 24th week of pregnancy, so that her figures are not strictly comparable with our own. Even taking this into account, however, the foetal mortality reported by White is incomparably lower than in any other large series of cases—a result which may well be due to the correction of abnormal hormonal levels in her patients.

Pre-diabetic Foetal Loss: Historical Review

Throughout this article the terms "pre-diabetic" and "diabetic" refer respectively to the phases before and after the diagnosis of diabetes.

Allen (1939) first drew attention to the abnormally high rate of foetal loss occurring in the pre-diabetic period. Mengert and Laughlin (1939) have reported a foetal loss rate of 29.8% in 84 pregnancies during this period. Diabetes developed before the menopause in all their patients. Miller, Hurwitz, and Kuder (1944) have analysed 252 pre-diabetic pregnancies occurring in women developing diabetes during the child-bearing period. Their figures, which are exclusive of abortions and miscarriages, and which therefore include only stillbirths, intrauterine deaths, and neonatal deaths, show a foetal loss of 19.8% during the 20-year pre-diabetic period in comparison with a non-diabetic control rate of 5.4%. The maximum foetal loss rate of 35.4% occurred during the five years immediately before the diagnosis of diabetes and was considerably higher than the foetal loss rate of 23.6% which occurred in the 93 pregnancies among the same group of women after the onset of diabetes. Miller (1945), analysing the obstetric histories of 57 women in whom diabetes was diagnosed after the age of 40, reported an overall pre-diabetic foetal loss of 8.3% rising to 15.8% in the 15 years immediately before the diagnosis of diabetes.

Henley (1947) found a loss of 18% in 160 pre-diabetic pregnancies. His survey covered the pre-diabetic phase of 46 women in whom the disease was diagnosed between the ages of 25 and 69. Dolger and Herzstein (1944) and Herzstein and Dolger (1946) have failed to substantiate these findings. The reports of these workers are based on the pre-diabetic histories of 200 married diabetic women, 94 of whom developed the disease before the age of 45. They conclude that, although there is a significant increase in the foetal loss rate during the five years immediately before the diagnosis of diabetes, yet for pre-diabetic periods of longer duration the rate is not significantly different from that of non-diabetic women. Miller (1946) has challenged this conclusion, and by applying the χ^2 test to their figures has shown the difference between the pre-diabetic foetal loss rate for the 15 years before the onset of diabetes and the control foetal loss rate to be statistically significant. The absence of a uniform definition of foetal loss rate throughout the literature makes precise comparisons of figures impossible.

We have also been impressed by the high rate of foetal loss characterizing the pre-diabetic histories of many of our patients. The present survey deals with the pre-diabetic histories of 165 women attending the diabetic out-patient department of the Royal Infirmary, Edinburgh. All patients were interviewed personally. The group was unselected, and represents 165 consecutive attendances of parous diabetic women at the department.

Present Investigation

Standard Rate of Foetal Loss.—The first step in this investigation consisted in establishing the foetal loss rate in a comparable group of non-diabetic women. This presented many difficulties. The report of the Registrar-General for Scotland is exclusive of abortions and therefore does not give figures of "total" foetal loss according to our definition. Equally unsatisfactory were the histories of patients admitted to local maternity hospitals, since the admission to such institutions is often limited to primiparous patients and to those developing complications of pregnancy. Our diabetic patients are drawn in almost equal proportions from urban and rural districts. Records from the city clinics were consequently not entirely comparable. The standard rate of foetal loss finally chosen for comparison was that of the non-diabetic women attending the Ayr County Maternity Service. This service caters for all pregnancies, normal and abnormal. Further, the patients are drawn from urban centres such as Kilmarnock and from the wide rural districts of Ayr County. Obstetric histories of 1,027 women admitted to the above service in 1942 were analysed. Among the 3,276 pregnancies involved there was a foetal loss of 263 (8%). The components of the foetal loss rate were as follows: abortions and miscarriages, 2.8%; stillbirths, 3.2%; deaths occurring in the first 14 days of the neonatal period, 2%.

Variables Affecting the Foetal Loss Rate.—In the case of non-diabetic women the foetal loss rate might be expected to vary with such factors as the social class and physical condition of the mother, the age of the mother at the time of pregnancy, and the number of previous pregnancies. In a strict analysis it would have been necessary to investigate the foetal loss rate corresponding to each of these variables and to each combination of variables. Such subdivision was, however, impracticable: apart from the difficulty of establishing definitions of social class and physical condition, the numbers involved when such subdivision was undertaken were too small to make statistical conclusions valid. It was assumed, therefore, that these variable factors were "randomized" in our data, and that they were homogeneous when any two rates of foetal loss were compared. The comparisons made above indicate that the foetal loss rate of 8% among non-diabetic women can be used as a satisfactory standard for comparison with the foetal loss rates of the diabetic women concerned in the present survey.

Results

The 165 patients involved were divided into two main groups: (1) insulin group—132 women in whom the administration of insulin was necessary for diabetic control; (2) non-insulin group—33 patients in whom dietary treatment alone was sufficient for diabetic control. Each group was subdivided into: (*a*) young diabetics—women in whom diabetes was diagnosed before the age of 45; and (*b*) old diabetics—women in whom diabetes was diagnosed after the age of 45.

TABLE II.—*Insulin Group—132 Insulin Patients*

Pre-diabetic Period	Total No. of Pregnancies	Foetal and Neonatal Loss	Foetal Loss Rate
0–2 years	20	10	50·0%
3–9 ,, ...	58	12	20·7%
10–19 ,, ...	129	21	16·3%
20+ ,, ...	252	29	11·5%
Total	459	72	15·7%

Insulin Group

Table II shows the pre-diabetic foetal loss rate in the 132 patients who were taking insulin. It will be noted that the overall foetal loss rate of 15.7% is similar to the 18% quoted by Henley and is twice the non-diabetic control rate of 8%. On the whole there is a progressive increase in the foetal loss rate as the time when diabetes was first diagnosed is approached. The foetal loss rate of 11.5% for pre-diabetic periods in excess of 20 years steadily reaches a maximum in the two years immediately before the diagnosis of diabetes. The foetal loss rate of 50% for the two-year pre-diabetic period in the present survey manifestly represents figures for young diabetics only, the last pregnancy among the old diabetics having occurred not less than four years before the diagnosis of diabetes.

TABLE III.—*Young Diabetics—59 Insulin Cases. Foetal Loss Rate According to Pre-diabetic Period*

Pre-diabetic Period	Total No. of Pregnancies	Foetal and Neonatal Loss	Foetal Loss Rate
0–2 years	20	10	50·0%
3–9 ,, ...	49	10	20·4%
10–19 ,, ...	45	9	20·0%
20+ ,, ...	10	1	10·0%
Total	124	30	24·2%

Young Diabetics.—Table III shows the pre-diabetic foetal loss rate among 59 young diabetics requiring insulin. It will be noted that the overall foetal loss rate of 24.2% in this group is three times the non-diabetic control rate of 8%—a ratio similar to that observed by Miller, Hurwitz, and Kurden (1944). Their foetal loss rate of 35.4% in the 1–5-year pre-diabetic period is comparable to the 50% during the 0–2-year period in our series, since we found the foetal loss rate of 50% in the 0–2-year phase to be substantially higher than that occurring in the 3–5-year period. We believe that the high foetal loss rate of the immediate pre-diabetic period is the characteristic feature of the pre-diabetic state, to be discussed later.

TABLE IV.—*Old Diabetics—73 Insulin Cases. Foetal Loss Rate According to Pre-diabetic Period*

Pre-diabetic Period	Total No. of Pregnancies	Foetal and Neonatal Loss	Foetal Loss Rate
3–9 years	9	2	22·2%
10–19 ,, ...	84	12	14·3%
20+ ,, ...	242	28	11·6%
Total	335	42	12·5%

Old Diabetics.—Table IV shows the pre-diabetic foetal loss rate among 73 old diabetics requiring insulin. An overall loss of 42 (12.5%) occurred in 335 pregnancies. As none of these women had been pregnant for at least four years before the onset of their diabetes, and usually for a much longer time, it is not surprising that they fail to show the very high foetal loss rate characterizing the immediate pre-diabetic phase of the young group of women. Miller (1945) reports similar observations.

TABLE V.—*Comparison of Foetal Loss Rate in Insulin and Non-insulin Cases*

	Insulin			Non-insulin		
	No. of Patients	No. of Pregnancies	Foetal Loss Rate	No. of Patients	No. of Pregnancies	Foetal Loss Rate
Young diabetics	59	124	24·2%	6	30	26·7%
Old ,,	73	335	12·5%	27	115	11·3%
Total ..	132	459	15·7%	33	145	14·5%

Non-insulin Group

The patients requiring only dietary treatment for the control of their diabetes form a small group of 6 young diabetics and 27 old diabetics (Table V). The overall foetal loss rate of 14.5% in this group is not significantly different from the rate of 15.7% in women requiring insulin. Subdivision of the non-insulin group into old and young diabetics revealed foetal loss rates not significantly different from those observed in the insulin group. The similarity in pre-diabetic foetal loss rates of patients requiring insulin and those controlled by dietary treatment alone has been commented on by Herzstein and Dolger (1946). There seems, therefore, to be no relation between the severity of the ensuing diabetes and the pre-diabetic foetal loss rate.

All comparisons of the foetal loss rates between the various groups and the control group discussed above have been subject to the χ^2 test and have been found to be statistically significant.

Discussion

Our observation of an abnormally high foetal loss rate for pre-diabetic periods of up to 20 years confirms the findings of Miller, Hurwitz, and Kuder (1944) and Miller (1945). Our observation of a maximum foetal loss rate among young diabetics in the years immediately before the diagnosis of diabetes still further confirms the findings of these workers.

The similarity of the foetal loss rate in the immediate pre-diabetic phase and in the post-diabetic period raises a doubt whether the immediate pre-diabetic period is in fact pre-diabetic. Herzstein and Dolger (1946) point out that the 0-5-year period is not wholly pre-diabetic, as it may include an unspecified number of undiagnosed diabetics, since it is never easy to determine the exact date of onset of diabetes. We cannot entirely accept this view, for the following reasons: first, in the majority of young diabetics the disease comes on acutely, leaving little doubt about its approximate date of onset; secondly, the features of diabetes, such as glycosuria, polyuria, loss of weight, etc., tend to be aggravated by pregnancy, and it therefore seems unlikely that had clinical diabetes been present during the 0–2-year period it would have been completely overlooked by the obstetrician in the majority of cases; lastly, and most important, Table III shows a significant increase in the foetal loss rate for at least a decade before the diagnosis of diabetes was made, and it is impossible to believe that these young patients were suffering from undiagnosed diabetes for as long as five years.

It seems, therefore, that there is a factor conducive to foetal mortality which may be active for as long as 20 years before the diagnosis of diabetes and very active for the immediately preceding five years. The precise nature of this factor still remains uncertain. It is probable that the factors responsible for the large babies, the high foetal loss rate, and the ensuing maternal diabetes have a common basis in some general metabolic disturbance in the mother, and that the features of clinical diabetes, such as polyuria, glycosuria, thirst, etc., are a very late stage of this metabolic disturbance, an early feature of which is a high foetal loss rate.

Summary

Insulin therapy has increased the fertility of diabetic women and has made pregnancy a relatively safe proceeding for the mother, but has failed to produce a very significant decrease in the foetal mortality rate in diabetic women.

The pre-diabetic obstetric histories of 165 women in whom diabetes was diagnosed between the ages of 25 and 69 have been analysed. The overall pre-diabetic foetal loss rate was twice the non-diabetic control rate.

In those patients in whom diabetes was diagnosed before the age of 45 the pre-diabetic foetal loss rate was three times the non-diabetic control rate. The maximum pre-diabetic foetal loss rate, which was six times the control rate, occurred in the two years immediately before the diagnosis of diabetes was made and was as high as that observed after the onset of clinical diabetes.

In those patients in whom diabetes was diagnosed after the age of 45 the pre-diabetic foetal loss rate, which in this group was one and a half times the non-diabetic control rate, failed to show the dramatic rise immediately before the diagnosis of diabetes observed in the younger group of women.

There appeared to be no relation between the severity of the ensuing diabetes and the pre-diabetic foetal loss rate.

The onset of clinical diabetes may be a late stage in some general metabolic disturbance an early feature of which is a high foetal loss rate.

We are greatly indebted to Mr. George Waugh, F.F.A., A.I.A., F.S.S., for his invaluable work, under the ægis of the Scottish Statistical Research Bureau, in collating and analysing the data in this paper, and to Dr. C. A. Bignold, Medical Officer of Health for Ayr County, for so kindly putting his maternity service records at our disposal.

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PREGNANCY COMPLICATED BY DIABETES MELLITUS

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During the past twenty years 45 patients with definite diabetes mellitus have been observed in 58 pregnancies at University College Hospital. The incidence was 1 in 580 deliveries. This high figure is due to the fact that a number of the patients were referred to the Obstetric Unit from the Diabetic Clinic of the hospital. Pregnancy in the diabetic is an infrequent occurrence, and is in part due to the decreased fertility of the diabetic patient and in part to the fact that diabetes is much commoner in women during the latter portion of the child-bearing period, when pregnancy is less frequent (Barns, 1941).

In 48 of the pregnancies diabetes had been diagnosed and treated by a physician before the onset of the pregnancy. In the remaining 10 pregnancies the diagnosis was made during the pregnancy on the strength of a fasting blood sugar of 130 mg. per 100 ml. or over, a typical blood-sugar curve, and history of diabetic symptoms. The diagnosis was subsequently confirmed after the pregnancy. Hence in approximately one-quarter of the patients pregnancy appeared to unmask the condition of diabetes by precipitating the onset of symptoms or actually to initiate the clinical onset of the disease, which persisted, although usually in a milder form, after the pregnancy in question.

*Working with a Lund Research Fellowship of the Diabetic Association.

Insulin Requirements During Pregnancy

In this series of 58 pregnancies treatment was with diet alone in 7 cases and with diet and insulin in 51. Of 19 cases under insulin treatment in which the diet remained unchanged throughout the pregnancy and the puerperium (alteration being made only during the labour), nine required more insulin as the pregnancy advanced up to the time of delivery; nine required more up to two to four weeks before delivery, after which a gradual and slight fall in insulin requirements occurred until delivery; and the remaining patient needed no alteration in the insulin dosage throughout pregnancy. Of the 19 patients 17 showed a marked fall in the insulin requirements after delivery; the other two showed no change. These figures support the contention that carbohydrate tolerance usually diminishes as pregnancy advances (Duncan and Fetter, 1934; Skipper, 1933).

It has been thought that any increase in the carbohydrate tolerance acquired during pregnancy was due to the transference of insulin from the foetus to the mother. Skipper (1933) reviewed the evidence and concluded that there was no good reason to believe that such improvement in the carbohydrate tolerance was due to this cause. It should be mentioned that eight of the nine patients who showed this improvement just before delivery were receiving oestrogen therapy at the time, and this may have some significance. Some writers claim that oestrogens improve the glucose tolerance in women developing diabetes at about the menopause (Gessler, Halsted, and Stetson, 1939; Spiegelman, 1940). Lawrence and Madders (1941), using small doses of stilboestrol on a few patients of menopausal age, failed to confirm these findings. In the present series the pregnant diabetics who were treated with oestrogens received ten times the amount of stilboestrol given to the patients of Lawrence and Madders.

The marked and abrupt fall in the insulin requirements after delivery in the majority of patients must be emphasized, for there is the obvious danger that the patient will develop hypoglycaemic coma if this fact is neglected.

Complications of Pregnancy

Hydramnios.—There appears to be a definite and pronounced tendency for the pregnant diabetic to develop hydramnios of the chronic variety with its added complications. In 17 of the pregnancies of this series clinical hydramnios developed—an incidence of 29%.

Coma.—One patient developed diabetic coma in the 33rd week of pregnancy and was successfully treated. Another was admitted with diabetic intoxication at the 29th week. This patient was never in diabetic coma, but her diabetes was exceedingly difficult to balance on account of repeated vomiting. She died a few days after admission. Her blood pressure was 170/100 one day before death, and on the day of death she developed epileptiform convulsions which were not hypoglycaemic in nature. At necropsy there was no evidence of eclampsia or nephritis. In some patients ketosis was precipitated by the onset of urinary infection.

Two patients developed hypoglycaemic coma, and there were others who experienced hypoglycaemic symptoms in the early stage of pregnancy. This may have been related to the development of renal glycosuria, which is often found in normal pregnancy and which may be superimposed on the diabetic condition, or to the prevalence of hyperemesis in early pregnancy or to overdosage with insulin. It cannot be stressed too strongly that the care of the pregnant diabetic should be shared with a physician who will supervise the treatment of the diabetes as soon as it is recognized.

Toxaemia of Late Pregnancy.—There is general agreement that the diabetic is more liable to develop late pregnancy toxaemia than the non-diabetic. The degree of this greater liability varies from three times (Mengert and Laughlin, 1939) to fifty times (White, 1937), according to different observers. On the strict standards for the classification of late pregnancy toxaemia adopted at University College Hospital, and previously outlined (Barns, 1941), there were 25 diabetic pregnancies with this complication. This gives an incidence of 43% as compared with the usual incidence of 35% obtained at University College Hospital for the non-diabetic pregnancies. The toxaemia in 12 of these 25 cases was severe enough to warrant admission to hospital, according to the standards laid down by Browne (1946). Hence the incidence of toxaemia of this severity is 20.7%, which is similar to that in diabetic pregnancies quoted by Herrick and Tillman (1938). The incidence of this severe toxaemia for all patients delivered at University College Hospital during the year 1939 was 5%. White (1935) found that the incidence of eclampsia in the diabetic was nearly 17 times that for the non-diabetic. It would therefore appear that the relative incidence of toxaemia of late pregnancy varies with the standard of severity taken for comparison, and that there is a predisposition for the pregnant diabetic to develop the more severe type of toxaemia.

Prognosis for the Mother

In the pre-insulin era a quarter of the mothers died during delivery or the puerperium and a further quarter died within two years of delivery (Williams, 1909; Offergeld, 1908). Diabetic coma was usually responsible for the maternal death. The prognosis for the mother has been considerably improved since the introduction of insulin. Skipper (1933) gave the immediate maternal mortality as 9.3%, with an additional mortality of 3.4% for the next two years. In the present series of 58 pregnancies in 45 diabetic patients there was one immediate death, to which reference has already been made above.

The diabetic is especially liable to infection of one kind or another. Provided that the diabetes is kept under proper control this tendency is reduced to a minimum. There were four pregnancies which were followed by puerperal pyrexia: two were due to urinary infection and one to pleurisy; the fourth was probably due to puerperal sepsis, but this was not definitely established by bacteriological investigation.

Walker (1927), like Skipper (1933), is of the opinion that if the diabetes is adequately controlled pregnancy does not produce a permanent increase in the severity of the condition. Observations made in this series of patients support that view. In 34 pregnancies the carbohydrate tolerance, as judged by the diet and insulin requirements before and after pregnancy, is known; in 28 (82%) it was unchanged and in six it was decreased. It is to be noted that the onset of the diabetes in these six patients occurred either within a few months of the beginning of the pregnancy or during the pregnancy (two patients).

Prognosis for the Foetus

The foetal mortality for pregnancies complicated by diabetes mellitus has remained persistently high in spite of the great advance made in the treatment of diabetes with insulin. In the pre-insulin era it was 41% (Williams, 1909). Since the introduction of insulin it has remained at approximately the same figure.

The obstetrical histories of the patients of the present series show that of 64 diabetic pregnancies 7 ended in abortion—an incidence of 10.9%. As judged from this small series it would appear that the incidence of abortion

in the pregnant diabetic is no greater than that in the non-diabetic (11.8%, Barns, 1947) or that in the woman who subsequently develops diabetes (Barns and Morgans, 1948). The high foetal mortality in the pregnant diabetic is therefore due to some unknown factor or factors which cause the death of the viable foetus and the newborn infant.

The 58 diabetic pregnancies have been divided into a first series of 43 and a second series of 15 because of a radical change in the treatment of the latter. Of the first 43 diabetic pregnancies two resulted in abortion, and in a third case the patient was evacuated (during the war years) whilst pregnant, and lost sight of. There are therefore 40 diabetic pregnancies which were followed throughout pregnancy and which continued beyond the 28th week. Of these 40 pregnancies 18 resulted in live infants, 13 ended in the birth of stillborn or macerated foetuses, and in the remaining 9 neonatal death occurred. The total late foetal mortality is therefore 55%. The cause of this high foetal mortality, consisting of intrauterine death of the viable foetus, stillbirths, and neonatal deaths, is little understood, and none of the hypotheses presented to explain it is wholly satisfactory.

Late pregnancy toxaemia in the mother, with its associated hormonal changes in the serum, has been considered by Smith *et al.* (1944) to be the cause of these foetal catastrophes. In the present series it was found that intrauterine death of the viable foetus did occur without the association of late pregnancy toxaemia, and also that neonatal death was infrequently associated with this complication in the mother. Conversely, Lawrence and Oakley (1942) found that toxaemia could exist without any accompanying foetal catastrophe. They found no support for the view that toxaemia was an important factor in the causation of the high foetal mortality in diabetic pregnancies. The foetal mortality for non-diabetic pregnancies complicated by late pregnancy toxaemia is approximately only half that for diabetic pregnancies with this complication (Barns, 1941). It would therefore appear that late pregnancy toxaemia cannot be regarded as the primary factor in the production of the high foetal mortality. The presence of this complication in the diabetic pregnancy cannot, however, be regarded as unimportant, for it may weigh the scales against a successful outcome.

Coma, diabetic or hypoglycaemic, has been incriminated in the past as a cause of intrauterine death of the viable foetus. Studies of pregnancies in women who subsequently develop diabetes have shown that there is a high foetal mortality in these pre-diabetic pregnancies which increases as the clinical onset of the diabetes is approached (Barns and Morgans, 1948; Miller, 1946). Presumably the factor responsible for these foetal deaths is the same but differs in degree before and after the onset of the diabetes, and it has been suggested that this factor might arise from the anterior pituitary lobe of the mother. It is therefore clear that if such is the case these diabetic complications cannot be the primary cause of the foetal catastrophe, for such occurs with undue frequency before diabetes develops.

Hypoglycaemia in the newborn infant has been suggested as an important cause of the high neonatal death rate in diabetic pregnancies. In six cases of the present series blood-sugar estimations of the newborn were carried out. In no case was the blood-sugar level below the normal range for newborn infants given by Ketteringham and Austin (1938), and in three of the infants so investigated neonatal death occurred. Hypoglycaemia therefore seems unlikely to be the cause of the high neonatal mortality rate, particularly as it is difficult to see why this condition should occur in the infant of the pre-diabetic, in whom there is also a high neonatal mortality rate. The blood-sugar level of the infant of the diabetic is higher than normal when *in utero* and at birth by virtue of the raised blood sugar of the mother. There is therefore an appreciable drop in the blood sugar to the normal range in the first few hours of life, and this fall is greater than is usual in infants of non-diabetic mothers. It therefore seems reasonable, and at least can do no harm, to give the infant glucose to allow this fall to be accomplished more slowly.

Infants of diabetic mothers are larger than normal; but so, too, are those born during the pre-diabetic period of the mother, hence hyperglycaemia in the mother cannot be the cause of the gigantism, as has been suggested. The abnormal hormone picture of high serum gonadotrophin, low serum oestrin, and diminished pregnandiol excretion sometimes found in these pregnant diabetics has been thought by White *et al.* (1939) to be related to the large size of the infant. This abnormal hormone picture had been claimed by Smith and Smith (1935a, 1935b, 1937, 1940) to precede the onset of, and to accompany, late pregnancy toxaemia. Since, however, the non-diabetic pregnancy with late pregnancy toxaemia does not produce the large infant characteristic of the diabetic mother, it seems unlikely that the abnormal hormone picture is directly related to the production of the large infant. Recently the importance of the pituitary gland in this connexion has been stressed, and it has been suggested that there might be an excess of the growth hormone from the maternal anterior pituitary lobe which causes the infant of the diabetic and the pre-diabetic mother to be large (Barns and Morgans, 1948).

The incidence of congenital defects of the foetus of the diabetic mother is greater than in the non-diabetic. Comyns Berkeley *et al.* (1938) state that the incidence for pregnancies in general is 3%. There were four infants with congenital defects out of the 40 diabetic pregnancies of the first series.

In view of the good results claimed by White (1947) for hormone therapy in the diabetic pregnancies it was decided to treat a series of diabetic pregnancies with oestrogens. The therapy was used on the assumption that oestrogens might act as an anterior pituitary lobe depressant. In the past it has been the custom at University College Hospital to terminate the pregnancy just after the 36th week in order to avoid intrauterine death. Although the infants obtained were large, they were immature. This immaturity cannot be neglected as a factor likely to increase the chances of neonatal death. The first series of 40 diabetic pregnancies were so treated.

The second series of 15 diabetic pregnancies have been treated with oestrogens, and early artificial termination of the pregnancy was avoided in all but the first two cases. There was one stillbirth due to cerebral haemorrhage which occurred in one of the pregnancies terminated early, one intrauterine death, and one neonatal death. Although the series is small, the results suggest that the outlook for the foetus of the pregnant diabetic is improved by the above procedures. It is hoped to present a detailed analysis of these cases in the near future.

Summary

A series of 58 diabetic pregnancies in 45 patients is reviewed.

In the majority of patients the carbohydrate tolerance was found to diminish as pregnancy advanced. In some, however, it increased prior to delivery, and it is possible that oestrogens given therapeutically may have been a factor in this improvement.

The tendency of the pregnant diabetic to develop hydramnios is confirmed.

It was found that hypoglycaemic symptoms and coma tend to occur in early pregnancy, and ketosis and diabetic coma in the latter part of pregnancy.

There is a greater tendency for the diabetic to develop late pregnancy toxaemia than the non-diabetic, and the relative incidence varies with the standard of severity of the toxaemia taken for comparison.

The maternal prognosis is good, and pregnancy does not make the diabetes worse provided that it is well treated.

The late foetal mortality was 5.5% in a first series of 43 pregnancies. In a second series of 15 pregnancies in which oestrogens were given there were only three deaths. The cause of the foetal mortality is discussed, and it is suggested that the factor affecting the viability of the foetus probably arises in the maternal anterior pituitary lobe. The incidence of abortion does not appear to differ from that for non-diabetic pregnancies, and suggests, first, that diabetes mellitus is not a cause of abortion, and, secondly, that the factor which reduces foetal viability exerts its strongest influence towards the end of pregnancy.

Congenital deformities, gigantism, and hypoglycaemia of the newborn are briefly discussed, and it is suggested that the tendency to gigantism is due to an excess of the growth hormone from the maternal pituitary gland.

We should like to express our gratitude to Professor W. C. W. Nixon, Director of the Obstetric Unit, for his encouragement and permission to make use of the case records of the Obstetric Unit; to Professor H. P. Himsworth, Director of the Medical Unit, for permission to make use of the records of the Diabetic Clinic and for helpful advice; and to Organon Laboratories for the generous supply of stilboestrol dipropionate.

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Another step towards closing the wartime gap in the issue of vital statistics by the Registrar-General has been taken with the publication of Part II of the *Statistical Review* for 1943. During that year in England and Wales the improvement in the birth rate following the record low figure in 1941 was maintained, the fall in the still-birth rate continued, and the number of marriages was the lowest for seventeen years. There were 684,334 live births during 1943, representing a birth rate of 16.2 per 1,000 total population. This maintained the improvement seen in 1942, when the corresponding figures were 651,503 and 15.6, and compared favourably with the record low figures of 579,091 and 13.9 for 1941. The birth rate for 1943 was the highest since 1930, when the corresponding figure was 16.3. Later figures showed that the birth rate further increased to 17.7 in 1944, fell to 15.9 in 1945, and again increased to 19.2 in 1946 and 20.6 (provisional) in 1947. Of the live births in 1943, 43,709 or 6.4% were illegitimate compared with 36,467 and 5.6% in 1942 and an average of 4.3% for the ten years 1930–9. In 1945 this proportion was 9.3%; in 1946 it was 6.6%, and in 1947 it was 5.3%.

THE RELATION OF STAPH. PYOGENES TO DENTAL CARIES

BY

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Appleton (1944), in his review of the bacteria occurring in dental caries, mentioned several workers who have isolated *Staphylococcus aureus* from carious cavities. Among them were Miller, Goadby, Kantorowicz, and Niedergesaess, but although they had established the presence of this organism in both the superficial and the deep layers of carious cavities it was only rarely and then in small numbers.

Nord (1946) stated that Gottlieb, in a private communication, said he had "discovered the micro-organism causing dental caries to be *Staph. aureus*, and that a perfectly sound tooth in a pure culture of this organism will in two months show caries which cannot be distinguished from true caries."

Gottlieb (1947) headed a paragraph of his book "*Staphylococcus aureus* produces dental caries," and referred to the work of Crawford (1946), who stated that *Staph. aureus* was isolated from carious cavities and that sterile extracted teeth, when placed in a culture of that organism, developed yellow spots and real cavities within two months. Ground sections of these teeth revealed exactly the same picture as that found in naturally carious teeth.

This paper reports the results of a collaborative investigation to test the claims of Gottlieb and Crawford and to find out if the presence of *Staph. aureus* in the mouth could be correlated with caries.

Bacteriological Technique

Material to be examined was incubated for twenty-four hours in a salt–meat medium specially selective for staphylococcus.* A loopful of this culture was spread on a horse-blood agar plate, incubated for twenty-four hours, and then allowed to age on the bench for two or three days so that colonies would have ample time to develop pigment. All varieties of colonies suspected of being staphylococcus were picked off and tested for the production of coagulase. Only "coagulase-positive" strains—i.e., *Staph. pyogenes*—were considered in the results which follow. These strains were all haemolytic. Most of them produced golden-yellow pigment (*Staph. aureus*), but some had white or nearly white colonies (*Staph. albus*). It has been well established that *Staph. pyogenes* nearly always liquefies gelatin and produces toxin and is potentially pathogenic for man. *Staph. pyogenes* should be regarded as including virtually all the strains which, on the basis of colour of colony, were formerly classed as *Staph. aureus*.

It has been shown that by the technique adopted it was usually possible to obtain a nearly pure plate culture of staphylococci when 300 staphylococci were mixed with 1,000,000 other bacteria in 1 ml. of a prepared mixture used as original inoculum. It follows that this method of culture gives no information about the presence or absence

*A full account of work on selective media for staphylococci is being published from the Department of Bacteriology.

of other bacteria, and that the results recorded in this paper refer only to staphylococci.

Experimental

1. *Exposure of Teeth to Cultures of Staph. pyogenes in vitro.*—Sound recently extracted teeth were macroscopically examined to confirm the absence of caries. They were boiled for half an hour and placed in a broth culture of *Staph. pyogenes*. This culture was renewed every two days and maintained at 37° C. Eleven teeth were treated in this way and exposed to the organisms for periods ranging from fifteen days to four months. None of the teeth showed any macroscopical change resembling caries, nor did there appear to be any reduction in the surface hardness of the enamel. Samples of the broth were tested at intervals for the presence of calcium, but none gave a positive result. Ground sections of the teeth made after exposure to the organisms did not reveal any microscopical change resembling caries.

2. *Attempts to Isolate Staph. pyogenes from Carious Cavities.*—Grossly carious teeth were extracted and a swab taken from the surface of the cavity was inoculated into the selective medium. The soft carious material was removed from the cavity with sterile excavators and a little of the carious material from the deep layers was inoculated similarly. Eleven teeth were examined; only one culture (from the surface) yielded *Staph. pyogenes*.

3. *Isolation of Staph. pyogenes from Mouth-washings and Attempts to Correlate its Presence with Caries.*—About 5 ml. of sterile nutrient broth was poured from a test-tube into the patient's mouth and instructions were given to let it wash round all the teeth for about 30 seconds. The broth was then run out of the mouth, through a sterile thistle funnel, back into the original test-tube, and 1 ml. was inoculated without delay into the selective medium. A careful "mirror and probe" examination of the mouth was made to ascertain the existence or absence of clinical caries.

The results of examining a group of 86 school-children aged 5-12 years are summarized in the accompanying Table. In 52 (27%) of 194 examinations caries was present when *Staph. pyogenes* was absent, thus constituting a frank disagreement.

Table Showing Results of Correlating Dental Caries with Staph. pyogenes in Mouth-washings

Date of Examination	No. of Children Examined	No. of Children with			
		Caries − *Staph.* −	Caries − *Staph.* +	Caries + *Staph.* −	Caries + *Staph.* +
16/7/47 ..	86	24	21	22	19
30/7/47 ..	7	—	1	1	5
10/10/47 ..	24	4	3	11	6
17/10/47 ..	28	4	10	4	10
24/10/47 ..	32	4	7	9	12
27/11/47 ..	17	—	—	5	12
Totals ..	194	36	42	52	64

The remainder may be said to have agreed. There is obvious agreement in 64 examinations (33%) where both were positive and in 36 (19%) where both were negative. There is some doubt in the 42 instances (21%) where caries was absent but staphylococci were present, but it could be argued that these were not in disagreement because the presence of *Staph. pyogenes* might be an indicator of early caries, undetected by the examination employed, which would appear later. Some such cases were in fact demonstrated.

All the children were examined on the first date and as many as possible were re-examined at intervals to test the constancy of findings in individuals and to note any onset of caries. On the whole the results were inconstant. Of 50 children twice examined 20 gave consistent findings, and of 20 examined three times only four were alike on each occasion. The disagreements were nearly always attributable to the bacteriological results; in only a few cases had caries developed during the interval between examinations. Among the children there were 10 with obvious caries who failed repeatedly to yield *Staph. pyogenes*. Nine children, however, who had no caries at the start but who harboured this organism did develop clinical carious lesions before their final examination.

In view of this last finding and the possibility that the presence of *Staph. pyogenes* in the mouth might be an indicator of incipient or early caries, examination was made of a further series of 17 selected patients who had a small pit or fissure which showed early clinical signs of caries. Nine also had gross carious lesions. Mouth-washings were cultured as before. A sterile probe was pressed firmly into the tiny cavity of the early lesions, care being taken to avoid contact with other tissues, and then used to inoculate the selective medium. Cultures from the deep layers of the gross lesions were also made. The results can be summarized as follows:

	Early Lesions	Gross Lesions	Mouth-washings
No. of examinations ..	17	9	17
Staph. pyogenes isolated	0	1	12

4. *Control.*—In order to test the possibility that *Staph. pyogenes* found in the mouth-washings might have come from sources other than the inside of the mouth, swabs were taken as indicated below and inoculated into the selective medium. Thirteen of the children referred to in Section 3 were examined, with the following results: (*a*) Swabs wiped over the lips and adjoining skin: none yielded *Staph. pyogenes*. (*b*) Swabs taken from the nostrils: three were positive. (*c*) Of the swabs from the tooth surfaces and gums, those that were positive coincided substantially with the positive mouth-washings.

Discussion

These investigations do not support the view that *Staph. pyogenes* causes dental caries or that its presence in the mouth is an indicator of active or incipient caries.

Exposing boiled teeth to cultures (Section 1) is an arbitrary procedure, under conditions very different from those occurring naturally in the mouth, and a negative result therefore may be regarded as having less significance than a positive one. Nevertheless, teeth were not attacked *in vitro* by *Staph. pyogenes*.

The failure to recover this organism from the lesions in early caries and also from the great majority of cavities in advanced caries using a sensitive selective culture medium is a point of considerable importance (Sections 2 and 4).

The evidence from culturing mouth-washings (Section 3) likewise does not support the association of *Staph. pyogenes* with caries. This organism is often present in the mouth irrespective of the existence of caries. In assessing the results shown in the Table a considerable percentage of examinations may be noted in which there was agreement between clinical findings and results of culture. There were also instances where the presence of *Staph. pyogenes* could be regarded as indicating the impending onset of caries. Against this, however, should be set the instances of frank disagreement, the inconstancy of recovery of *Staph. pyogenes* from individuals on repeated examination, and the number of those who had caries but repeatedly failed to yield *Staph. pyogenes*.

In an earlier series of 25 dental students examined similarly there was possibly suggestive evidence for the idea that *Staph. pyogenes* in the mouth might correlate with the existence of caries, but the further evidence presented here showed that this could not be substantiated.

If *Staph. pyogenes* does not produce caries it is unlikely that other staphylococci will do so. As indicated earlier in this paper, the strains known as *Staph. aureus* would

practically all be included in those designated *pyogenes*. Other staphylococci are less proteolytic and saccharolytic on substrates usually tested in culture, and are less haemolytic and toxigenic. They would therefore be less likely than *Staph. pyogenes* to be concerned in the aetiology of caries.

Conclusion

A combined clinical and bacteriological investigation using a highly sensitive and selective medium for the isolation of *Staph. pyogenes* has failed to reveal an aetiological relationship between this organism and dental caries.

We desire to express our thanks to Mr. R. Bradbury, school dental officer, Borough of Stretford, for arranging and assisting with the examination of the children. We also acknowledge our indebtedness to Professor H. B. Maitland, Director of the Department of Bacteriology.

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SENILE DETERIORATION OF THE CENTRAL NERVOUS SYSTEM

A CLINICAL STUDY

BY

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Comparatively little has been written about the clinical aspects of neurology in the aged. Even textbooks dealing with old age, such as those of Thewlis (1946) and Stieglitz (1943), are unsatisfactory. The best account at present is that of Macdonald Critchley (1931). He notes the frequent occurrence of several clinical changes. Diminution of objective pain sensation is mentioned, while complaints of subjective pains are said to be common. Progressive loss of vibration sense is stated to be customary, while sluggish pupils, missing superficial reflexes, and weak or absent tendon-jerks are said to be the usual findings. No indication is given, however, of the frequency of these signs or of the age at which they may be expected.

Since the absence of reflexes and alterations of sensation might give rise to the misdiagnosis of neurological lesions, it seemed expedient to examine a series of healthy old people to ascertain what variations are normal. I therefore examined 200 Chelsea pensioners. Most of these men were known to me both personally and professionally, so that considerably more co-operation was forthcoming than might otherwise have been the case. This should add to the credibility of the clinical findings. Among the pensioners examined a small number were found to have neurological lesions previously unrecognized: these were omitted from the series. The results of the clinical examination of the nervous system are described below.

Motor Changes

Tendon Reflexes.—Each case was tested for supinator, triceps, biceps, knee, and ankle jerks. Only 7% of those examined had every reflex present, these being in the younger age groups. The arm-jerks were normal in all men under 70, but the ankle-jerks were not elicited in over half the cases even at this age. In those over 70 there was a definite drop in frequency of all reflexes, but no further decrease until the age of 85 except in the ankle-jerks (Table I).

TABLE I.—*Percentage of Tendon Reflexes Obtained*

Age	No.	Supinator		Biceps		Triceps		Knee		Ankle	
		R.	L.	R.	L.	R.	L.	R.	L.	R.	L.
65–69 ..	16	100	100	100	100	100	100	87	87	43	38
70–74 ..	57	67	65	88	88	70	72	79	77	32	35
75–79 ..	72	69	68	84	85	84	84	76	76	32	35
80–84 ..	31	68	65	90	90	87	80	80	80	12	12
85–91 ..	9	33	33	66	66	44	55	44	44	22	22
Mean values ..		69	63	86	87	79	79	77	77	29	31

Superficial Reflexes.—Contrary to expectation, the vast majority of plantar responses were normal. Age did not seem to have any bearing on the frequency of abnormality, which was 5%, mainly scattered in the age groups between 70 and 84. There was no difference between the two sides of the body, except in three pensioners. The abdominals, however, were elicited less regularly. The upper quadrants always responded more easily than the lower ones, but there was no constant difference between right and left sides of the belly. The average for all the men was less than 50%, with a drop at 70 years of age and another drop after 85, similar to that found in the deep reflexes (see Table II).

TABLE II.—*Superficial Reflexes*

Age	No.	Abdominals		Plantars	
		R.	L.	R.	L.
65–69 ..	16	100% 63%	100% 75%	100%	95%
70–74 ..	57	54% 51%	49% 52%	96%	94%
75–79 ..	72	47% 36%	45% 40%	96%	96%
80–84 ..	31	61% 42%	48% 35%	89%	87%
85–91 ..	9	22% 0%	22% 0%	100%	100%

Power.—Power was assessed only roughly in the absence of a dynamometer. The pensioners were graded by strength of grip and by power of flexion and extension at elbow and knee. The results were classified as very good, good, fair, and poor. Loss of strength seemed to develop with increase of age, but this was not universally true in the cases examined, as may be seen in Table III.

TABLE III.—*Power in Limbs*

Age	No.	Very Good	Good	Fair	Poor
65–69 ..	15	40%	33%	27%	0%
70–74 ..	54	13%	62%	20%	5%
75–79 ..	66	8%	39%	45%	8%
80–84 ..	31	16%	29%	32%	23%
85–91 ..	8	0%	37%	50%	13%
Means :		13%	44%	34%	9%

Sensory Changes

Vibration Sense.—As changes in vibration sense were among the positive findings noted by earlier observers considerable care was taken in testing for this form of sensation. Bony points on both wrists, elbows, shoulders, ankles, knees, shins, and the sacrum were tested. The percentage registering on the sacrum was uniformly small in every age group. More than 90% appreciated vibration on the bones of the upper extremity. Ankles and shins showed perception in over 70% of cases, but the knees appreciated the sensation in just over 50%. The results are shown in Table IV.

TABLE IV.—*Percentage Registering Vibration Sense*

Age	No.	Wrists		Elbows		Shldrs.		Ankles		Shins		Knees		Sacrum
		R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	
65–69 ..	16	100	100	100	100	80	94	87	87	94	87	50	56	12
70–74 ..	57	100	100	100	100	98	98	88	84	81	79	61	67	18
75–79 ..	72	100	100	100	100	90	89	76	73	73	74	51	53	15
80–84 ..	32	97	97	94	97	94	94	62	56	62	44	31	34	10
85–91 ..	9	100	100	100	100	100	100	89	89	67	78	67	78	11
Mean:		99	99	98	99	94	94	79	76	75	72	52	56	15

Joint Sense of Position.—The sense of position of joints was tested by moving the great toe on each side. Three tests were made for each toe after a period of irregular movement. The vast majority of patients showed normal position sense in the feet (Table V).

TABLE V.—*Position Sense of Toes*

Age	No.	Abnormal Right	Abnormal Left
65–69	16	0%	0·5%
70–74	56	4%	3%
75–79	72	2%	3·5%
80–84	33	1%	1%
85–91	9	0%	0%

Nose-Touching.—To my surprise quite a number of the pensioners were unable to touch their noses accurately when their eyes were closed. The resulting movement was not an intention tremor but a definite dysmetria. This was usually present in both hands, but if one alone was involved the left was the site of occurrence more often than the right. Up to the age of 85, increasing years had no effect on the frequency of the abnormal findings (Table VI).

TABLE VI.—*Dysmetria in Touching Nose*

Age	No.	Right	Left	Both
65–69	16	0%	25%	19%
70–74	56	9%	14%	20%
75–79	72	11%	14%	18%
80–84	33	6%	15%	21%
85–91	9	0%	0%	44%
	Mean:	8%	15%	20%

Rotation of Wrists.—This test showed normal results in four-fifths of the men examined. When there was difficulty in carrying out the movements both wrists were equally at fault. The difficulty appeared to be one of performing an unfamiliar series of muscular exercises and not a cerebellar dysfunction. It is significant that the disability percentage increases steadily with the age of the pensioners tested (Table VII).

TABLE VII.—*Difficulty in Wrist Rotation*

Age	No.	Defective
65–69	16	0%
70–74	56	4%
75–79	72	25%
80–84	33	33%
85–91	9	44%

Pain, Temperature, and Light Touch.—The results of examination for these sensations were often very hard to interpret. Sometimes pain and temperature sense would be diminished over the same area. Sometimes one would be normal while the other seemed impaired. Touch was involved only half as often as the other sensations. Altogether some 45 patients failed to register 73 sensations between them. The findings were most frequent in the age groups between 70 and 85. The sites of anaesthesia were fairly constant, being almost always on either the shin or the forearm. Usually the inner aspects of the limbs were involved, but the distribution seemed to follow more of a cord segmental pattern than to conform to any actual superficial nerve area. As it is not possible to summarize this information satisfactorily in the form of a table, let me state that 24% of the men showed impairment of one kind or another. Two-fifths of these did not register pain, two-fifths did not register changes in temperature, and one-fifth could not appreciate light touch. Deep pain sensation was not tested in this examination.

Cranial Nerves

In the examination of the cranial nerves, Nos. 1, 2, and 8 were omitted. The only abnormality detected, apart from changes in the pupils, was an external rectus palsy in two cases. The reactions of the pupils were, however, often abnormal. Sometimes they reacted to light alone, sometimes to accommodation alone, often to neither. A small pupil was more common than a dilated one, but the proportion of either was not great enough to impress the observer.

TABLE VIII.—*Percentage of Positive Reactions of the Pupils*

Age	No.	Light		Accommodation		Neither	
		One	Both	One	Both	One	Both
65–69 ..	16	6	69	0	69	6	12
70–74 ..	57	9	60	0	60	9	25
75–79 ..	72	12	54	7	36	10	24
80–84 ..	32	3	50	0	19	3	44
85–91 ..	9	0	33	0	0	0	67
	Mean:	9	54	3	41	8	28

It will be seen from Table VIII that if a response is lost it usually disappears in both pupils. Even at the earliest age group nearly one-third of the men had lost either light or accommodation reaction. The percentage of failures to react increases steadily with age, being more complete in the case of accommodation. A completely inactive pupil was found in two-thirds of those over 85.

Discussion

What is the meaning of the findings recorded above? Let us first try to make a rough statement about the anatomical location of some of the lesions which are indicated. This is not easy, for they appear to be very widely scattered in their distribution.

Judging by the plantar response it would appear that the pyramidal tract is affected in less than 5%, since some of the responses considered abnormal were not of true Babinski type. The frequent absence of the tendon reflexes would suggest possible cord lesions at varying levels. With regard to the sensory losses, it would seem that sensations passing in the lateral spinothalamic tract are lost twice as often as those conducted by the ventral one. A discrepancy appears, however, when the various posterior column sensations are examined. Position sense is normal in the feet of nearly all those examined. Yet vibration is often not felt in the sacrum, ankles, and knees. Dysmetria in the arms is not uncommon. It seems hard to reconcile such findings anatomically. In the same way, the variations in response of the pupils to light and accommodation, tending to become more frequent with advancing years, suggest a progressive but patchy dissolution. It is possible, of course, that some of these lesions may be functional and not organic. For example, it has been shown that the incontinent bladder of old age can be brought under conscious cerebral control by suitable treatment in a number of cases.

The most important result of the investigation, however, is the wide variation of "normal" findings in old age.

Until this is appreciated, non-existent disease of the central nervous system will frequently be suspected or even diagnosed. I have often seen clinical combinations suggesting tabes dorsalis or progressive muscular atrophy in pensioners who were really healthy. Doubtless others have had a similar experience.

Summary

The results of neurological examination in 200 healthy Chelsea pensioners are given.

Absent pupillary reactions, missing tendon-jerks, and superficial reflexes were common motor findings.

Absent vibration sense in sacrum and lower limbs, dysmetria, and patchy analgesia in the forearms and shins were not unusual.

Anatomical location of lesions accounting for such findings was difficult or impossible.

The possibility of misdiagnosis owing to such results of senile deterioration is stressed.

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Medical Memoranda

A Case of Tetanus in a Child

Recovery from tetanus, though not unduly uncommon, merits being reported, especially when there are additional interesting and unusual features in the case.

CASE REPORT

A boy aged 8 was admitted at 1.30 p.m. on June 9, 1947. The receiving officer diagnosed "generalized peritonitis ? cause." On June 7 the boy fell down and hurt his left leg and his chest. Shortly afterwards he had pain in the abdomen, which became very severe during the night of June 8. There was no nausea or vomiting. The doctor who first saw him found some rigidity and tenderness of the abdomen and diagnosed intestinal obstruction.

On admission the receiving officer observed "absolute rigidity." When I saw the patient, he was flushed and looked ill; pulse 110, temperature 99° F. (37.2° C.), respiration 26, laboured and with working alae nasi. He had marked fetor oris and a furred tongue. The abdomen was a little tender in the left hypochondrium and right iliac fossa; there was no guarding or rigidity. Nothing abnormal found in chest. Several bruises on left leg, recent scratches on front of right chest, and an old healing abrasion over the right knee were seen. He had no neck rigidity or any difficulty in voluntary movement of limbs, but severe pain on attempted movement of trunk. Back very stiff and lumbar muscles tender. Rectal examination revealed nothing abnormal. Blood count within normal limits. Acetone and a trace of sugar were found in the urine.

At 5 p.m. he could not open his mouth wide enough for inspection of the throat, and the attempt produced a painful spasm of the abdominal muscles. On interrogation he remembered some difficulty in opening his mouth the previous evening. A tentative diagnosis of tetanus was suggested, and became evident at 7.15 p.m. with risus sardonicus and typical generalized painful spasm, most pronounced in the abdominal muscles. Treatment was started at 7.30 p.m. with 5 dr. (19 g.) of paraldehyde (in saline) per rectum with 1/200 gr. (0.32 mg.) of atropine subcutaneously. A.T.S. 120,000 units (in two doses) intravenously, and 100,000 units (in three doses) intramuscularly, was given, also 300,000 units of penicillin (in wax). Next day paraldehyde was administered at suitable intervals by the intramuscular route and penicillin was continued. Fluids were taken well and urine was passed. Orthotonus and risus sardonicus were well marked, and occasional generalized spasms were still occurring. Next day the pain became more severe and pethidine had to be given as well as paraldehyde. June 12: trismus still marked, but only one generalized spasm occurred. June 13: general rigidity more pronounced than previously; severe pain in both legs, but no spasms; some cutaneous irritation. June 14: well-marked serum rash; still much pain in abdomen, chest, and legs, but no spasms. June 19: trismus less; general improvement definite; solid food started. June 24: no more pain; rash subsided. On June 29 he got up and on July 5 was discharged home.

The boy received 120,000 units of A.T.S. intravenously and 100,000 units intramuscularly in the six hours following diagnosis, 21 dr. (82 g.) of paraldehyde per rectum in the 18 hours following diagnosis, and 65 ml. of paraldehyde by intramuscular injection administered over the next 11 days (average 5.9 ml. a day; maximum actually given in 24 hours was 19 ml.). In addition he received 1,700 mg. of pethidine hydrochloride (including 100 mg. orally) in eight days (average 212.5 mg. a day; maximum actually given in 24 hours, including 50 mg. orally, was 300 mg.). A total of 6,900,000 units of penicillin was administered in 21 days. All this actually entailed 96 needle punctures. The old abrasion on the right knee (which was considered to be the portal entry of the infection rather than the recent scratches on the chest) was dressed for about two days with a hydrogen peroxide dressing.

COMMENT

This case has certain curious features. Most notable is the fact that it presented itself as an acute abdomen, and the first two doctors who saw him diagnosed in succession an acute intestinal obstruction and acute generalized peritonitis. The misleading history of a fall within 48 hours of onset raised the possibility of a ruptured spleen or of an osteomyelitis of the vertebral column. The general appearance and laboured breathing suggested the presence of a pneumonia. Risus sardonicus did not become evident until about 24 hours after the first appearance of trismus (which at no time prevented the boy from speaking distinctly or drinking) and only a very short period before the onset of generalized spasms. Pethidine appeared to give much relief, definitely more than paraldehyde, especially after the appearance of the serum rash (which started four days after the administration of A.T.S. and took 11 days to subside without any special treatment). The patient remained throughout quite bright and co-operative.

I wish to thank Mr. John Scholefield for permission to publish this case, Dr. Dynski-Klein for her help in establishing the diagnosis, and Dr. Rilstone for admitting this child into my ward.

N. N. IOVETZ-TERESHCHENKO, F.R.C.S.

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Dystocia after Amputation of Cervix

The Manchester operation for prolapse is carried out so often that it is well to record any untoward results. Hunter (1939) drew attention to the occurrence of dystocia and abortion after the operation and urged conservation of the cervix in the child-bearing period. However, the occasional case does occur in which pregnancy follows extensive operation.

CASE REPORT

In November, 1938, a patient, then aged 40, was treated by anterior and posterior colphorrhapy and amputation of the cervix for procidentia. The cervix was grossly lacerated and hypertrophied, so that the amputation was maximal. There had been four children, all delivered by forceps, and subsequent pregnancy was not anticipated. The cure was complete, and the menstrual cycle was not altered except that the periods were rather scanty.

In September, 1944, the patient's doctor (Harold Hirsch, of Stockport) sought her admission to hospital. He stated that she had been two days in labour, and that although the head was well down in the pelvis he could distinguish no external os on vaginal examination. This examination was repeated in hospital, with the same findings. The head was separated from the examining finger by a thin sheet of muscle in which there seemed to be no aperture. Lower-segment caesarean section was carried out immediately. On exploring the lower pole of the uterine cavity from above no internal os could be found, but there was a definite dimpling where the muscle seemed very thin. After closing the abdomen, vaginal examination was carried out with antiseptic precautions. No blood was present in the vagina, nor could any be expressed. The thin area mentioned above was identified and deliberately perforated with the finger, after which lochia drained freely.

The puerperium was satisfactory, the lochia being normal for a caesarean case—i.e., rather scanty. Vaginal examination was repeated on the 17th day, when again no external os could be identified. Obviously some orifice must have survived the first operation, otherwise neither menstruation nor conception could have occurred. It is suggested that cicatrization had reduced it to a very small aperture, and that the swelling consequent upon the hypervascularity of pregnancy had completed the closure.

WALTER CALVERT, M.R.C.O.G.

REFERENCE

Hunter, A. J. W. (1939). *British Medical Journal*, **2**, 991.

Reviews

BREAST-FEEDING

Breast Feeding. A Guide to the Natural Feeding of Infants. By F. Charlotte Naish, B.A., M.B., B.Ch. Oxford Medical Publications. (Pp. 151; illustrated. 10s. 6d.) London: Geoffrey Cumberlege. 1948.

Paediatricians look a little uncomfortable, even blush, when the subject of breast-feeding is mentioned. They all proclaim and extol its importance; but it is a complicated problem which has not received sufficient scientific and practical study, and it is therefore sadly mismanaged in practice. In this book Dr. Charlotte Naish gives the fruits of her own study and clinical practice, her aim being to provide general practitioners, midwives, and health visitors with a practical guide in their supervision of breast-feeding. She has succeeded in her aim. Her book is of outstanding merit, and deserves the attention of all who are concerned with the feeding of young infants; it ought to take its place as a standard and authoritative guide to breast-feeding.

The main part of the book is a practical account of breast-feeding in its various phases, from the antenatal preparation for it, throughout the critical stages of its beginning and establishment, to its end in weaning. The author emphasizes the details and technique of management and fully describes them, relating them to the underlying physical and chemical processes at work in the mother and child; she describes these briefly in the first three chapters, and also gives a clear account of the thoughts and feelings of the nursing mother. In this preliminary section the author lays down a principle or working rule that "the baby must be adequately fed, and as much of its food as possible must come from the breast. The younger the baby the more important breast-feeding is." The author regards this rule as of overriding importance, and it governs every part of her practice and almost every page of her book. As a result she says much about and gives instructions for complementary feeding, its indications throughout breast-feeding, and the technique of its administration. There are separate chapters on the succeeding phases of breast-feeding, the first week, the second week, the danger weeks (third and sixth), established breast-feeding, and weaning. Then follow chapters on breast trouble and the contraindications to breast-feeding, with a final and useful chapter on breast-feeding without suckling, where she discusses cases of prematurity, cleft palate, and pyloric stenosis.

The present low standard of practice in breast-feeding is mainly due to downright ignorance, the bad tradition of nursery lore, and the lack of serious clinical study. Dr. Naish's book should do much to remove these obstacles. Based on extensive clinical experience, it is rich in clinical observations. Moreover, it is a constant search for links between the clinical phenomena she describes and the underlying physiological and chemical processes that produce them; and it is this fusion of clinical observations with their hidden causes that determines the techniques of management. Her style is clear, concise, and simple; there is not the slightest difficulty in understanding what the author means in her arguments, explanations, and directions, and she has also at her command a quiet irony which can clear the ground of debate like a stick of dynamite. This is an excellent and admirable book. It should serve its immediate purpose in raising the standard of practice in breast-feeding. It ought also to call the attention of physicians and physiologists to a rich and comparatively unworked field of clinical and scientific study—human lactation and infant digestion.

CHARLES MCNEIL.

GROWTH OF THE MIND

Emotional Problems of Living. By O. Spurgeon English, M.D., and Gerald H. J. Pearson, M.D. (Pp. 438. 16s.) London: George Allen and Unwin. 1947.

To describe the dynamics of the mind to the ordinary intelligent reader is as difficult as describing the structure of the atom without using mathematics. The former seems easier, because all people are in daily touch with mental problems in themselves and in others, but the processes involved in the development of mental patterns in normal character and in neurosis can be clearly understood and accepted only through a first-hand knowledge of the technique of psycho-analysis as well as its formulated doctrines and hypotheses. Nevertheless, it is possible to convey much information on mental development which can be of use to students, teachers, and nurses. The authors have attempted to do this—with considerable success—using the Freudian doctrine of emotional development from babyhood onwards.

In fairly simple language they take the reader through an account of the various stages of instinctual development in so far as it is basic to the structure of the ego and the unconscious. They describe the vicissitudes of the instincts in the oral, anal, and phallic stages, then through the latent period to adolescence. They write with great care and simplicity and include short illustrative case histories. Those phases are rather rigidly distinguished, which is not the case in reality, for they interpenetrate one another. Furthermore, they do not emphasize enough the role of ego development in the light of the conflict between impulse and conscience, nor the fact that most of these processes are strictly unconscious in their dynamic relations. They do not discuss Melanie Klein's work on the early formation of the conscience and the development of infantile depression, despite its controversial character. The book is such easy and entertaining reading that the novice and the unwary may be easily swept away; it is a big book, and so readable that they may come away too easily instructed in the most difficult of all human problems.

EMANUEL MILLER.

SURGICAL UROLOGY

Surgical Urology. In two volumes. By Dr. G. de Illyés, Professor of Urology and Director of the Clinic of Urology in the Hungarian Royal Péter Pázmány University, Budapest. (Pp. 679; 391 illustrations. 63s.) London: Constable and Co., Ltd. 1948 (1942).

Professor G. de Illyés is a well-known Continental urologist and this book is the outcome of his long personal experience. Volume 1 is divided into a general and a special part. In the former the author discusses symptomatology, methods of examination, and the special instruments used in urology, and in the latter diseases of the kidneys. In Volume 2 he considers the rest of the genito-urinary tract and ends with an interesting chapter on disturbances of sexual function. An index for both volumes is included. The book is profusely illustrated by 391 figures, many of which are in colour; it is clearly printed and well bound, and the text is enriched by descriptions of individual cases to emphasize important facts. The chapters on the kidney and urethra are particularly good, though we do not agree with all the author's views.

This work first appeared in 1942, but the war delayed its publication in England until now; as a result, the author does not entirely fulfil his wish "to present urology in its present advanced stage of development." He does not discuss the most recent advances in urology and describes the sulphonamides (which are not indexed) as a new drug, and their efficacy in the treatment of urological infections is left undecided. He has tried to make the book encyclopaedic in scope and has therefore had to expound some subjects briefly. It would be an advantage to have details of how to carry out transplantation of the ureters into the colon. Diagrams illustrating operative technique might be more plentiful throughout. In the description of suprapubic removal of bladder papillomata we find no mention of protecting the wound surfaces by towels soaked in antiseptic (e.g., silver nitrate) to prevent implantation metastases.

Nevertheless, in spite of these criticisms, the work represents the results of enormous labour in clinical observation and surgical achievement, and the author is to be congratulated on the successful accomplishment of his task. If a new edition is prepared and the most recent advances in urology added, together with a bibliography and an index at the end of each volume, it could be whole-heartedly recommended and would find a permanent place in our reference libraries.

DAVID AIKEN.

BRITISH HOSPITALS

British Hospitals. By A. G. L. Ives. (Pp. 50; with 4 plates in colour and 26 illustrations in black and white. 5s.) London: Collins. 1948.

Mr. Ives's contribution to the series "Britain in Pictures: the British People in Pictures" is well worthy of its place in this deservedly popular set of volumes. The story is felicitously told and the illustrations illuminate the text. In fifty pages he covers the history of hospitals from A.D. 600 to 1948. He uses examples surviving in our midst to bring alive the compassionate spirit imbuing those who founded and those who worked in them; a spirit that waxed and waned, but always survived vicissitudes of national and social upheaval; an inspiration the author hopes and believes will persist even after the transformation recently undergone.

After a storied chapter on the mediaeval scene, with Christian piety as the motive force behind the monastic foundations, he passes on to discuss the royal hospitals and the dawn of scientific medicine; thence the eighteenth century and the spate of voluntary hospitals, listing twenty-eight in the provinces built between 1736 and 1798, besides those in London. He naturally makes much of the Nightingale era, and does not forget the great service of John Howard in for ever harping on cleanliness. There is then a chapter on "The Turn of the Century," with mention of Osler's textbook, the coming of *x* rays, the development of bacteriology, the realization of the social aspects of medicine, the advent of the almoner, and the establishment of the King's Fund. Then follows a judicious appreciation of the conditions and circumstances that led up to a general recognition of the need for a unified hospital system and of the stages which culminated in the National Health Service. The frontispiece is a fine initial from the illuminated cartulary of St. Bartholomew's; there are pictures by Anna Zinkeisen, Felix Topolski, Edward Ardizzone, and many reproductions of old pictures and engravings. This is quite a fascinating story for the general reader, and there is a lot, too, that will be new to many who thought they knew all about hospitals.

E. ROCK CARLING.

THE PATIENT'S VIEW

Taking the Cure. By Robert G. Lovell, M.D. (Pp. 93; illustrated. $2 or 10s.) New York and London: The Macmillan Company. 1948.

This book, written by an ex-patient, is primarily intended to be handed to the newly admitted patient to a sanatorium so that he shall learn the nature and purpose of what lies ahead of him. I accordingly tried it out on a number of sanatorium patients and asked them what they thought of it. Unanimously they condemned it as a futile attempt to convey in two hours' reading what can be learned and understood only by being *lived through* for weeks and months: "As misleading as programme notes on an unfamiliar piece of music—although perhaps factually accurate," said one. "It tells you nothing that you don't pick up all in good time from doctors, nurses, and other patients," said another, adding, "Surely if anyone is curious enough to want to read the subject up he would want something a bit meatier." "Isn't it a bit optimistic?" asked yet another with feeling. "There's no mention whatever of failed A.P.s, fluid, and similar disappointments that seem to be more the rule than the exception during the course of treatment."

Apart from perpetuating the classical misconception that in lateral decubitus the lower lung does less work than the upper, the book is incontrovertibly accurate—as far as it goes. Unfortunately for us, it is only too evidently written for the average patient in a far-off happy land where dire shortage of nursing and domestic staff does not discourage (if not positively preclude) his ringing a bell whenever he wants a book from his bedside table—rather than raise his shoulders from the bed. The text is enlivened with six line drawings—one showing cross-sections of the chest, one showing plan and elevation of a very useful reading rack, and four that are more facetious. There are also appendices on "Leisure Time Reading," "Listening to Classical Music," and on playing that engrossing paper-game of "Battleships."

GEORGE DAY.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

The W. H. Ross Foundation (Scotland) for the Study & Prevention of Blindness. (Pp. 236. 3s.) London: University of London Press. 1948.

A history of the Foundation, and papers on research carried out under its auspices or at its request.

Tramp Royal. By R. MacMahon. (Pp. 315. 10s. 6d.) London: John Langdon. 1948.

The travels of a doctor to remote countries.

Osteoperiostitis Tuberculosa y Sifilitica. By V. B. Olives. (Pp. 403. No price.) Barcelona: Ediciones Byp. 1948.

A monograph on the pathology, diagnosis, and treatment.

Études Chimiques sur la Tuberculose. Edited by J. Paraf. (Pp. 130. 300 francs.) Paris: L'Expansion Scientifique. 1948.

A collection of papers reviewing work with antibiotics and chemotherapeutic agents.

La Mesure du Rendement Circulatoire. By A. H. Israel and C. H. Rendu. (Pp. 75. 200 francs.) Paris: L'Expansion Scientifique. 1948.

The authors propose a formula for determining circulatory efficiency from the blood pressure and pulse rate.

Abhandlungen der Deutschen Akademie der Wissenschaften zu Berlin. By H. Nachtsheim and H. Klein. No. 5. (Pp. 71. M. 750.) Berlin: Akademie. 1948.

This number contains a monograph on erythroblastosis foetalis.

Estudio Clinico del Enfisema Pulmonar. By J. A. Sciuto. (Pp. 164. No price.) Montevideo: Rosgal. 1948.

A monograph on the pathology, diagnosis, and treatment of pulmonary emphysema.

Leitfaden der bakteriologischen Trinkwasseruntersuchung. By H. Beger. 2nd ed. (Pp. 122. M. 6.60.) Berlin: Urban and Schwarzenberg. 1948.

A short account of the bacteriological investigation of water

Therapeutisches Taschenbuch. Edited by G. Ruepp. (Pp. 394. 12 Swiss francs.) Berne: Hans Huber. 1948.

A summary of therapeutics for students and house-men.

Synopsis of Physiology. By A. Rendle Short, B.Sc., M.D., F.R.C.S., and others. 4th ed. (Pp. 346. 20s.) Bristol: John Wright. 1948.

A summary intended chiefly for medical students.

Human Embryology and Morphology. By Sir Arthur Keith. 6th ed. (Pp. 690. 40s.) London: Edward Arnold. 1948.

The text has been revised for this edition and many new references have been added.

Das Gesundheitswesen in der Bauplanung Berlins. By P. Vogler and G. Hassenpflug. (Pp. 95. No price.) Berlin: Werner Saenger. 1948.

Public health statistics and maps.

Le Fond d'Oeil des Hypertendus et des Cyanoses. By D. Routier. (Pp. 100. 1,350 francs.) Paris: Masson. 1947.

Annotated illustrations of the ophthalmoscopic appearances.

Contemporary Religious Jurisprudence. By I. H. Rubenstein. (Pp. 120. $2.50.) Chicago: Waldain Press. 1948.

Discusses the American law in relation to faith healing, fortune telling, and pacifism.

Chirurgie Moderne de la Hanche. By R. Charry. (Pp. 316. 1,340 francs.) Paris: G. Doin. 1948.

An illustrated practical manual on the surgery of the hip-joint.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JANUARY 8 1949

EPILEPSY

During the last 25 years great additions have been made to our understanding of epilepsy, but there is perhaps no other field of medicine where so large an increase of knowledge has left so many problems still unsolved. This may be, at least in part, because the accumulation of new facts has outrun our capacity to interpret them. The Lumleian Lectures delivered by Dr. F. J. Nattrass and published in this and the previous issue of the *Journal* are therefore timely, for he has made a wide survey of a topic which is of importance to workers in many departments of medicine.

These two lectures raise many questions of absorbing interest. One of the most fundamental is the relationship between consciousness and the functions of the brain. Why does a patient lose consciousness in one kind of epileptic attack and not in another, and what, if any, is the connexion between loss of consciousness and cerebral dysrhythmia? Many neurologists have believed that there are one or more localized areas in the brain disturbance of which causes loss of consciousness. The interpretation of clinical experience by means of electro-encephalography certainly affords some support for such a view. Adrian[1] has pointed out that electro-encephalography shows that in some epileptics considerable areas of the cerebral cortex may be involved in an abnormal rhythmical activity for some time before or after the attack in which consciousness is lost. "That the mind can still function with abnormal waves in much of the cortex," Adrian says, "is not more remarkable than that it can still function when half the cortex is giving the regular beat of the α rhythm or when a large part is removed by the neurosurgeon. What seems to be necessary is that some part of the cortex should still be free to react to the incoming messages from the sense organs and to those handed on from other parts of the brain." We may perhaps infer from this that if a cerebral dysrhythmia is to produce loss of consciousness primarily by disturbing the functions of the cerebral cortex it must be extremely widespread, and such a disturbance, affecting in its course the motor areas, will cause a generalized convulsion, or in other words will produce the clinical picture of grand mal. Clearly, if this view is correct, there must be some other explanation of epileptic attacks characterized almost exclusively by loss of consciousness such as petit mal, or by loss of consciousness accompanied by a sudden fall, as in akinetic epilepsy or what are sometimes called "drop attacks." Again, it is evident that the physiological disturbance is not identical in petit mal and in akinetic epilepsy. In akinetic epilepsy the loss of consciousness may be so brief as to be demonstrable only by the most careful questioning of the patient, for it may be limited to the period of the fall itself. This contrast between the tolerance which the cerebral cortex shows to widespread electrical disturbances in dysrhythmia of the grand mal type and the sudden short and selective loss of consciousness in petit mal and akinetic epilepsy suggests that there must be areas of the brain especially intimately associated with consciousness, and it is tempting to suppose that these areas may be functionally related to the recently discovered system of suppressor bands, from which electrical stimuli evoke a widespread suppression of cortical activity.

This again raises the much-discussed question of the relationship between epilepsy and narcolepsy. Dr. Nattrass would separate the two decisively on clinical grounds, and there is no doubt that as a rule narcolepsy, whether or not accompanied by cataplexy, can be distinguished without any difficulty from epilepsy. Nevertheless there appear to be intermediate states in which the distinction is more difficult. Loss of consciousness is common to both narcolepsy and many forms of epilepsy; similarly, loss of muscular power and tone is common to cataplexy and akinetic epilepsy. The tempo of the disturbance is different, and this may be nosologically important, but the anatomical pathways and physiological functions are surely akin. From the patient's point of view the differences may well be much more significant than the resemblances, but the neurophysiologist may find that each will illuminate the other.

Hughlings Jackson's division of the symptoms of lesions of the nervous system into the negative phenomena of loss of function and the positive phenomena produced by functions released from higher control was a fertilizing idea of the utmost value in the development of neurological thought, but recent advances in our knowledge of epilepsy show its limitations. Can what has been termed a "discharging lesion" be explained entirely as a manifestation of the disappearance of higher control? And is there no place, between functions lost and functions released, for the conception of a distortion of activity? In any case epilepsy is a disruptive and disintegrating influence, for its positive manifestations occur at a comparatively low level of nervous organization. The epileptic convulsion does not consist of co-ordinated movements: these depend upon combinations of neurones too highly organized to be susceptible to stimulation by a method as coarse as an epileptic dysrhythmia.

For all our new knowledge of cortical electronics the essential nature of epilepsy still eludes us. Why does the synchronous electrical discharge occur? Electrical convulsant therapy has shown, what indeed had been stated on theoretical grounds before, that anyone will have an epileptic fit if appropriately stimulated. Nevertheless, the technique of the electrically induced convulsion has also shown that individuals vary greatly in their susceptibility to epilepsy. This fact, of course, was well known to clinicians. A brain injury or a cerebral tumour will induce fits in one person but not in another, and this difference does not appear to depend upon differences in the nature or

[1] Adrian, E. D., *The Physical Background of Perception*, p. 79. Oxford, 1947.

situation of the lesion. It has been shown statistically, however, that it does depend, to some extent at least, upon heredity. Sufferers from traumatic epilepsy, for example, have a much higher incidence of epilepsy among their relations than controls, and many investigations have shown that from one-quarter to one-third of all patients with idiopathic epilepsy have epileptic relatives. But we do not know what constitutes the hereditary predisposition, nor even in what part of the body to search for it. Perhaps, during recent years, students of epilepsy have been too much preoccupied with the nervous system. Humoral factors have been studied in the past without much result, yet they still force themselves upon the attention of every neurologist. Why do so many female epileptics have fits predominantly, or even exclusively, at their menstrual periods? Why does hydration tend to precipitate attacks and dehydration to diminish their frequency? How does the blood-sugar level influence the incidence of convulsions, and to what is the benefit of a ketogenic diet due? These and many similar biochemical questions illustrate the practical and theoretical importance of metabolic factors. Moreover, all our effective therapeutic agents, being chemical, must be made humoral before they can act. All that we have learned about epilepsy in recent years can still be fairly described as a knowledge of what happens when things go wrong. We have been elaborately and successfully recording the speed of a galloping horse that has escaped from the stable door. All our pharmacological remedies are at best little more than strings with which we tie up the door, and which the horse from time to time breaks. But the door has a lock, and we have still to find the key.

DIABETES AND PREGNANCY

Before 1921 the occurrence of pregnancy in a diabetic woman was a medical curiosity; in those days amenorrhoea was the general rule among such women, as indeed it still is while the diabetes is uncontrolled. The diabetic woman who did succeed in becoming pregnant ran a serious risk of death during the pregnancy, during labour, or in the following year or two: overall maternal mortality figures of 50% have been recorded. The foetal mortality was also high, not far short of 50% for the entire pregnancy and neonatal period. The discovery of insulin by Banting and Best in 1921 and its application to the control of diabetes mellitus has had a remarkable influence on the fertility of diabetic women and on their maternal mortality. Diabetes is no longer a rare complication of pregnancy, or, from the physician's point of view, pregnancy a rare complication of diabetes, and with proper control the maternal mortality has been reduced to about 1 or 2%. On the other hand, to quote from the paper by Dr. J. A. L. Gilbert and Professor D. M. Dunlop which appears elsewhere in this issue, "In spite of the most stringent medical and obstetric supervision our foetal loss rate during the last five years has been as high as 51.4%." This figure, which agrees with those of many other authors, including Mr. H. H. Fouracre Barns and Dr. M. E. Morgans, whose paper on this subject is also published in this issue of the *Journal*, makes it painfully evident that control of the diabetes with insulin and diet has no influence whatever on the foetal mortality.

Control of the diabetes itself during pregnancy is now for practical purposes largely a solved problem, and the fact that different regimes based upon differing conceptions of the changes in carbohydrate metabolism during pregnancy all produce satisfactory results so far as maternal mortality is concerned indicates that close co-operation between physician and obstetrician is all-important—a point stressed by Barns and Morgans. How to improve the foetal mortality, then, is the pressing problem, and the solution of this is still awaited.

The high rate of foetal loss found in the pregnancies of women who subsequently develop diabetes—becoming increasingly obvious as the interval between pregnancy and the onset of the diabetes shortens—was first observed by Allen[1] in 1939 and has since been reported by several other authors.[2-4] Gilbert and Dunlop publish figures which are in close agreement with these writers. In the pre-diabetic as well as the diabetic period this high foetal mortality is caused by an excess of late intrauterine and neonatal deaths, the abortion rate having been found by Barns and Morgans to be essentially the same in non-diabetic, pre-diabetic, and diabetic women. It is clear, then, that neither the hyperglycaemia nor the ketosis of diabetes can be held to account for the adverse effects on the foetus, since the foetal death rate is high before the diabetes makes its presence clinically detectable, while proper control of the diabetes does not reduce it. On the other hand, there is general agreement that the incidence of toxaemia of late pregnancy is significantly increased in diabetes, in spite of adequate control of the latter. Smith and his colleagues[5] consider that the hormonal changes in the serum which they believe to take place even before the onset of toxaemia may be responsible for the foetal catastrophes. On the supposition that the harm is done by a lowering of the blood oestrogen and progesterone White[6] has treated a series of some 300 consecutive diabetic pregnant women with oestrogens and progesterone and has obtained 90% foetal survival (excluding deaths before the period of viability).

This striking success has not yet been confirmed, nor are the premises upon which the method of treatment is based generally accepted, though in fairness to Smith and his colleagues it must be admitted that their researches have never been properly repeated by other observers. There is no doubt, for example, that intrauterine death of the viable foetus can occur in the absence of late pregnancy toxaemia, while, conversely, Lawrence and Oakley[7] found that toxaemia did not necessarily cause foetal death. Palmer and his colleagues[8] have recently treated 42 consecutive cases of pregnant diabetic women along the lines advised by White and reported a foetal survival in 36 cases of 81.3%,

[1] *Amer. J. Obstet. Gynec.*, 1939, **38**, 982.
[2] Mengert, W. F., and Laughlin, K. A., *Surg. Gynec. Obstet.*, 1939, **69**, 615.
[3] Miller, H. C., Hurwitz, D., and Kuder, K., *J. Amer. med. Ass.*, 1944, **124**, 271.
[4] Barns, H. H. F., and Morgans, M. E., *J. Obstet. Gynaec. Brit. Emp.*, 1948, **55**, 449.
[5] *Amer. J. med. Sci.*, 1944, **208**, 25.
[6] *Penn. med. J.*, 1947, **50**, 705.
[7] *Quart. J. Med.*, 1942, **11**, 45.
[8] *W. J. Surg. Obstet. Gynec.*, 1948, **56**, 175.
[9] *Amer. J. med. Sci.*, 1939, **198**, 482.
[10] Barns, H. H. F., Lindan, O., Morgans, M. E., and Swyer, G. I. M., *Proc. Soc. Endocrinol.*, 1948–9 (in press).

compared with 60% for a previous group of 41 patients not treated with stilboestrol and progesterone. When, however, the χ^2 test is applied to these figures a value of 2.762 is obtained, which means that the difference between the treated and untreated groups could have occurred in random sampling more frequently than once in 20 times, so that the significance of the reported difference is in some doubt.

Foetuses from diabetic mothers have a marked tendency to be overweight; that this is not the result of maternal hyperglycaemia is shown by the fact that the same tendency is seen during the pre-diabetic period, while control of the maternal diabetes does not decrease the mean weight of the foetuses. It has been suggested by White and her colleagues[9] that the abnormal hormonal levels in the blood already mentioned might be responsible for the large size of the foetus; it is well known, however, that late pregnancy toxaemia in non-diabetic mothers is associated with underweight rather than overweight babies, so that this explanation seems unlikely. In seeking a more plausible theory to account for the observed facts Barns and Morgans[4] have suggested that increased production of the diabetogenic growth-promoting complex of the anterior lobe of the pituitary might be the factor which is responsible for the increased size of the foetus and for the late foetal catastrophes, as well as for the development of the diabetes. They further suggest that the effectiveness of oestrogens, if they produce the results claimed by White, lies in their ability to inhibit the anterior pituitary. Some experimental work lends support to the first part of this hypothesis, for the administration to pregnant rats of an extract of ox anterior pituitary lobe containing the diabetogenic growth-promoting complex has been found to produce up to 100% of stillbirths, depending upon the dosage.[10]

Whether or not either of these theories is correct, it would seem that an investigation is urgently required to compare the effects on foetal mortality of (1) no specific treatment directed towards saving the foetus, (2) termination of the pregnancy (usually by caesarean section) at the 36th week to avoid the late foetal deaths, (3) oestrogen treatment combined with termination, and (4) oestrogen treatment alone. It seems probable that termination of pregnancy has failed to reduce the overall foetal mortality because, while many late intrauterine deaths are avoided, it has increased the neonatal death rate due to prematurity (in spite of the large size of the infants). To be of real value, oestrogens—or any other therapeutic agents—must be able to avert late intrauterine death and so enable full-term birth to occur, with its much reduced likelihood of neonatal death.

NEW YEAR HONOURS

The medical profession will warmly applaud the great honour bestowed on Sir John Boyd Orr, F.R.S., one of the newly created barons. As director of the Rowett Research Institute, Aberdeen, he had a world-wide reputation in nutritional science, and between the wars did much to shake the complacency of those who believed that the people of Britain were well fed. Feeling, no doubt, the need for a bigger platform to urge forward his views, inspired by a determined idealism, he entered Parliament as an Independent after a by-election for the Scottish Universities in 1945. "I stand," he said then, "for a world food policy of production for consumption and distribution according to needs, just on the lines of the Hot Springs recommendation." Busy as he was, he at the same time acted energetically as the chairman of the B.M.A. Committee which drew up *A Charter for Health*, published in 1946. Sir John was re-elected to Parliament in the general election in 1945. Within a few months he was appointed Director-General of the United Nations Food and Agriculture Organization, and shortly after this resigned his seat in Parliament. His fearless and consistent advocacy of his views as Director-General of F.A.O. earned him world-wide admiration. It is good to know that the country will have the benefit of his wisdom in the debates of the House of Lords.

Three medical men have been designated Knights Bachelor. Professor Henry Cohen is Professor of Medicine in the University of Liverpool and vice-chairman of the Central Health Services Council. He rendered outstanding service to the B.M.A. as chairman of the Medical Education Committee, whose report was published last year. Professor Sydney Smith is Regius Professor of Forensic Medicine and Dean of the Faculty of Medicine in the University of Edinburgh, and his name is familiar as the author of a famous textbook. Mr. H. E. Griffiths is surgeon to the Albert Dock Hospital, London, and has done pioneer work in the rehabilitation of disabled persons.

Sir William Gilliatt has been raised from C.V.O. to K.C.V.O. Sir Wilson Jameson has been created G.B.E. Dr. Edith Summerskill, M.P., is to become a Privy Councillor. Many other honours have been deservedly bestowed on medical men and women, a full list appearing elsewhere in this issue.

"ANTRYCIDE"

"Antrycide" is a new synthetic preparation which appears to mark an important advance in veterinary medicine. The Under-Secretary of State for the Colonies, Mr. D. R. Rees-Williams, and the heads of the Pharmaceutical and Agricultural Divisions of Imperial Chemical Industries at a meeting at the Colonial Office on Dec. 29 gave some details about the use of this drug in the prevention and treatment of trypanosomiasis in cattle in tropical Africa. It was stated that trials in East Africa had demonstrated that a single treatment will cure cattle infected with *T. congolense* and *T. vivax*, and that it has been used with success against *T. brucei* infection in cattle, horses, and dogs, *T. evansi* in camels, and *T. simiae* in pigs. Experiments are still proceeding, but it is apparently possible to protect cattle against *T. congolense* for from four to six months in the majority of cases, and against *T. vivax* for a rather shorter period. Certain cases in which the disease has "broken through" after a shorter period are being investigated. *T. congolense* is the most harmful trypanosome affecting domestic animals in most parts of East Africa. Among cattle in British West Africa *T. vivax* is more important than *T. congolense*. It was further claimed that "antrycide" has no toxic effects, and that its administration by hypodermic injection is so simple that the presence of a veterinary surgeon is not necessary. At the same time, Mr. Rees-Williams said that there would probably be a greatly increased demand for veterinary surgeons in these parts of Africa because of the stimulus which would be given to cattle-rearing following the diminution of the ravages of the tsetse fly.

The supplies of the new drug, which it is hoped will amount to two or three tons this year, sufficient to protect 2,000,000 animals, will be limited at first to Government veterinary departments, those in Kenya, Uganda, and the Sudan having priority, following which field trials will be undertaken in West Africa. The research which led to the

discovery of "antrycide" has occupied four years. It has been undertaken by a team of I.C.I. chemists and biologists working first in experimental laboratories in Manchester and later in parts of Africa where trypanosomiasis is endemic, the work being based on laboratories in Khartum, Nairobi, and Entebbe, Uganda. The team was headed by Dr. F. H. S. Curd, Ph.D., who tragically was killed in a railway accident over a month ago. He, with Dr. D. Garnet Davey, Ph.D., another member of the team, jointly discovered "paludrine," the antimalarial drug, for which they were awarded the Society of Apothecaries' gold medal in 1947. A third member of the team was Dr. W. A. Sexton, Ph.D.; and the fourth, the only medical member, was Dr. Charles Melville Scott, who is at present in Africa and, before he became head of the biological department of I.C.I., was lecturer in materia medica at Edinburgh University.

The drug—a white crystalline powder soluble in water—is the result of that type of research in the new field of heterocyclic chemistry which has been described as "enlightened empiricism." A great number of compounds were tested, first of all in this country on trypanosome-infected mice, and later on cattle in Africa. After many failures a substance was discovered which had a slight effect on the disease, and then attention was directed to stepping up the potency. Ultimately the most effective preparation was found to be the one now presented, the serial number of which was M.7555. In reply to a question about how the drug worked, Dr. Cecil Cronshaw, group director in charge of the Pharmaceutical Division of I.C.I., simply said, "We do not know." The tests in Africa, which began a year ago, have been carried out in collaboration with the Tsetse Fly and Trypanosomiasis Committee of the Colonial Office, and further details from this committee and from the I.C.I. team will be awaited with interest.

RESISTANT STAPHYLOCOCCI

It is now common knowledge that strains of staphylococci resistant to penicillin are being encountered with increasing frequency, particularly in hospital practice, where cross infection accounts for their spread. Dr. Mary Barber, who reported a year ago in this *Journal*[1] that the proportion of such strains encountered among staphylococci isolated from actual lesions had risen in successive periods from 14.1 to 38%, now describes a more recent series of investigations in which the proportion of resistant strains isolated from a variety of sources in the same hospital has reached 59%.[2] It is noteworthy that two of these were cases of septicaemia: both patients died in spite of intensive penicillin treatment, and a positive blood culture was obtained from one of them when, owing in part to renal inadequacy, the blood penicillin content was no less than 8 units per ml. This paper also contains further interesting data bearing on the mode of origin of these strains and a discussion of the recently suggested idea that contact with other bacteria may restore their sensitiveness—unfortunately resistant strains were even commoner in mixed than in pure cultures, a finding which lends no support to this hypothesis.

Almost all staphylococci found to be naturally resistant to penicillin (as distinct from those artificially habituated to high concentrations *in vitro*) produce penicillinase, an enzyme which destroys the drug. The formation of this enzyme can be detected by the appearances in a primary culture in a "cup" or "ditch" plate. Barber mentions the observation made originally by Waterworth[3] that colonies of such an organism attain full or even abnormally large size at the boundary of the inhibition zone; having destroyed the penicillin in their neighbourhood they can grow unimpeded. The possibility of studying this and other phenomena connected with antibiotics by such exceedingly simple methods has perhaps discouraged more exact quantitative study. That a good deal can be gained by applying more exact methods is shown in the work of Gilson and Parker,[4] who have defined a unit of penicillinase and devised a method for its accurate assay. They were thus able to determine the amount formed by 40 strains of staphylococcus. Twenty-two formed little or none, but the quantity formed by the remainder varied from 190 to 125,000 units per g. of culture. These findings gain their chief interest when compared with the results of a double test of sensitivity to penicillin, one employing an inoculum of only a few hundred cells and the other of 10,000 times that number. Except in the case of two strains a small inoculum of a penicillinase-forming organism was usually inhibited by quite a low concentration of penicillin, often not exceeding that required by a normally sensitive organism. On the other hand, a large inoculum of a penicillinase-forming organism grew in concentrations a thousand or more times greater, the degree of difference generally corresponding with the amount of enzyme formed by it. Thus, as these authors say, the "resistance" exhibited by the organisms is "an artefact introduced by the method of testing: it expresses simply the ability of the resting cell to dispose of the penicillin in its environment."

Gilson and Parker are not the first to point out that the size of the inoculum requires control in such a test, but their very thorough investigation emphasizes this necessity; indeed it seems to demand from the laboratory a much more searching investigation of the properties of a staphylococcus than has ever been contemplated hitherto if the probable effect of penicillin on it is to be predetermined. The results of treatment in, say, a case of septicaemia are likely to depend not only on whether penicillinase is formed but in what amount; and the possibility of clearing the blood stream, where there may be few bacteria, may be indicated by the results of a sensitivity test employing a small inoculum. That there is perhaps yet another factor, although it may only apply to comparison between different bacterial species, is suggested by the observations of Bondi and Dietz.[5] They also studied the effect of inoculum size on the sensitivity to penicillin of Gram-positive penicillinase-forming bacteria and obtained similar results, but they found that the degree of variation did not depend on the total quantity of penicillinase formed but on the rapidity with which it was formed in the early stages of growth.

[1] *British Medical Journal*, 1947, **2**, 863.
[2] *Lancet*, 1948, **2**, 641.
[3] *Ann. Inst. Pasteur*, 1948, **75**, 94.
[4] *J. Bact.*, 1948, **55**, 801.
[5] Ibid., 1948, **55**, 843.

DEATH AT BIRTH

As the Registrar-General recently pointed out,[1] certification of the causes of death is at its least precise at the two ends of the age scale. Relatively few necropsies are performed after still-birth or neonatal death, yet the need for accurate information about the numerical importance of the various sources of danger to infant life is increasingly felt. The downward trend in infant mortality rates in recent years is the result of a decrease in the death rate in the later stages of the first year of life. The still-birth and neonatal death rates have, it is true, shared in the general improvement, but the rate of decline has been much slower among infants either at birth or in their first month of life.

[1] *Registrar-General's Statistical Review of England and Wales for the Years 1938 and 1939 (Text)*, 1947. H.M.S.O., London.
[2] *Amer. J. Obstet. Gynec.*, 1947, **54**, 188.

In preventive action the concentration of effort should be during the dangerous first month. Effective action, however, depends on accurate information which, in this context, only post-mortem dissection can give. A recent report from the Bellevue Hospital, New York, is therefore to be welcomed, for in this Labate[2] summarizes the necropsy results in 78% of the 1,114 foetal and neonatal deaths occurring in the hospital during the ten years between 1933 and 1943. The four major causes of death were found to be prematurity, pulmonary lesions, birth trauma, and maceration (following antepartum or intrapartum death, often of unknown origin). Prematurity, the most important cause, accounted for 27.6% of the deaths among the cases examined—a finding consistent with previous studies of this type. Necropsy in such cases usually shows a generalized immaturity of the vital organs of the body. The maldevelopment of the lungs causes persistent cyanosis; renal function is inefficient because glomerular development has not been allowed to go on as usual to the thirty-sixth week; the alimentary tract is immature; and heat regulation is unstable. The four main objectives in the care of the premature child must therefore be the maintenance of body temperature, the prevention of cyanosis, proper nutrition, and the prevention of infection. The problem of prematurity must concern the obstetrician as much as the paediatrician; he must delay the onset of labour, be sparing in the use of sedatives, minimize the strain of the second stage by episiotomy and by low-forceps delivery, and be ready to apply vigorous measures of infant resuscitation after birth.

The plight of the premature child is often made worse by coexistent defect. Pulmonary lesions were a cause of death in 21% of viable premature babies on whom a necropsy was performed. Pneumonia was a particular hazard in the neonatal period, and 80% of the deaths due to this disease were the result of aspiration pneumonia. Among full-term infants, too, pulmonary lesions due to aspiration of amniotic fluid, pneumonia, haemorrhage, or cystic disease were the most frequent cause of death. Birth trauma, however, also accounted for many deaths in this group. Injuries were of three main types—intracranial, spinal, and intra-abdominal. Difficult operative delivery appeared to be the most frequent cause of injuries, the nature of which partly depended upon the maturity of the infant. Lacerations of the dura and subdural haemorrhage were the lesions most frequently found among full-term infants, while subarachnoid and subventricular haemorrhages were more common in premature infants. Spinal dislocations were apt to follow difficult breech delivery, and abdominal injuries such as rupture of liver were sometimes the result of too strenuous attempts at resuscitation in the premature.

Labate remarks that the value of surveys of post-mortem findings is to be judged by the lowered mortality rate which results from an application of the lessons learned. By that standard the fall in the death rates among infants delivered at the Bellevue Hospital in the ten-year period under review is an indication that these lessons have been successfully translated from the post-mortem table to the delivery room and the nursery.

WORLD PROGRAMME OF DISEASE PREVENTION

Every year the International Health Division of the Rockefeller Foundation publishes a report on its activities of special interest to health officers and other workers in the field of public health. The report for 1947 covers the world from China to Peru. In China the Division has started a programme of malaria control and research on typhoid fever; in Peru it is carrying out special studies on the development of local health services. Two important subjects discussed are the continued prevalence of malaria in many parts of the world and progress in the control of yellow fever. Yellow fever is being studied under the auspices of the Division in East and West Africa and in many South American countries, and malaria in Italy and Sardinia, the Netherlands, the West Indies, and South America.

One rather ominous feature is remarked in connexion with the malaria control measures instituted in Italy. After a D.D.T. house-spraying campaign carried out in a coastal region north of Naples and in the Tiber delta it was found that, in contrast to previous experience, house flies were not affected. Apparently a race of flies abnormally resistant to D.D.T. has become predominant in these areas and also in other regions of the mainland where the insecticide has been in use for several years. Thus far all varieties of anopheline mosquitoes remain susceptible to D.D.T., and malaria transmission rates continue very low in controlled areas, but the general sanitary value of the spraying is lessened.

Another field of study is typhus fever. Experiments here have included the testing of para-aminobenzoic acid in the treatment of epidemic louse-borne infection, and the preparation has been found to have a distinctly favourable effect as regards duration of fever, incidence of complications, and mortality, though there are certain contra-indications and the treatment is not always effective. Work is also being done on mice to find chemicals of value against the organism of scrub typhus.

On the general question of health care a representative of the International Health Division has undertaken a survey of international trends which took him to 12 countries. He noticed three major defects in the planning and legislation for medical services. The most serious was the complete failure, except in Australia, to consider the categories and numbers of personnel and their training required to establish the organization envisaged by the legislation. Another defect was that, except in South Africa, planning and legislation were for sickness rather than for health insurance. Finally, he found inadequate provision for the three chief lacks in medical care to-day—namely, chronic, mental, and rehabilitation services. Two other minor defects were disclosed: that in most countries planning had proceeded without reference to what was developing in other countries, and that the need for auxiliary medical personnel was almost completely disregarded. The United States, and to a lesser extent Canada, were the only countries in which the training of auxiliary personnel, apart from nursing, had been standardized with the level of training controlled by a national organization—but it is evident that the observer failed to notice what has been and is being done in Britain in this connexion. The same investigator calls attention to the backwardness of medical education so far as concerns the training of the general practitioner in preventive medicine, geriatrics, psychosomatic medicine, and rehabilitation; but it is added that because of its new Health Act Britain has a great opportunity of exploring and demonstrating the positive aspects of health.

The Rockefeller Fellowships are an important branch of the work of the Foundation. In 1947 the International Health Division directed the studies of 112 individuals to whom fellowships had been granted. Of these 112 the main interests of 65 were in public health administration. Nearly all of them were studying in educational institutions in the United States or Canada, but a few were engaged in field activities. The Fellows came from 26 countries, only one of them from England. The report is a great record of world endeavour complementing that of the World Health Organization.

THE PROBLEM OF AGEING

BASIC DIFFICULTIES OF RESEARCH

BY

V. KORENCHEVSKY, M.D.

(From the Oxford Gerontological Research Unit, Oxford)

Great interest in the problems of gerontology is being shown in medical and scientific circles and by the public at large. Misunderstandings on the subject among non-specialists, however, are sometimes considerable. Therefore a summary of some of the main difficulties of the problem and of gerontological research might be of interest to those who have no time to study the matter in detail.

Theories of Senescence

There are several theories of senescence. Professor Warthin (1929, p. 160) sums up his critical review in the following pertinent words: "In general they are all built upon insecure foundations, hypothetical substances and hypothetical changes that may be due to the processes [effects, V.K.] of senescence and not its cause. Not a single one of all these theories of senescence so far offered has a leg to stand upon; for the greater part they are pure hypotheses constructed about some single fact."

Professor Medawar (1946), in his conclusions, is equally emphatic: "The problems of old age and natural death are hardly yet acknowledged to be within the province of genuine scientific inquiry." He emphasizes that the gerontologist requires many accurate data, scientifically controlled, for his conclusions; he has no time for "anecdotes" and loose statements, such as those concerning very old age in some animals and human beings, various sweeping theories of senescence, etc. He rightly says that the present-day gerontologist is quite aware of the fact that he has to begin "the study of the problem of ageing from scratch," and that gerontologists "would first of all try to piece together a full empirical description of the phenomenon of ageing as it is reflected in structural changes of tissues and cells and, more particularly, in the type and intensity of tissue and cellular metabolism. Only scraps of such information are now available."

The theory recently suggested by Bab (1948) belongs to the same category as defined by Warthin: in this theory one of the two factors on which, according to him, ageing depends is the diencephalon, about which so far we know comparatively little, and the changes in which most probably are the effects of ageing and not one of its primary causes.

Thus it is clear that, until the main facts concerning this problem are discovered and pieced together by experimental and clinical research, gerontologists will not be able to construct any reliable theory of senescence.

Pathological Character of Present Ageing

The greatest difficulty, however, of gerontology is that we know practically nothing of normal physiological senescence and the normal span of life. Referring to man, Mueller-Deham and Rabson (1942) state that, "in the first place, the old patient is a sick one; and, secondly, the sick patient is an old one." The latter sentence would be more correct in a modified form: "and, secondly, the sick patient is ageing more rapidly."

It is obviously impossible to discover normal features and establish normal standards of physiological senescence unless normal individuals are available: they should possess the best hereditary characters, should live a normal span of life in normal conditions of nutrition and environment, and should be free from any disease that might leave after-effects on their tissues and organs.

It is clear that from this point of view those centenarians who are available at present are deficient in various respects for human gerontological research. To begin with, we do not know whether 109–112 years, the longest span of human life so far registered with reasonable accuracy (Korenchevsky, 1947), really is the longest one and cannot be extended further under those more normal conditions of existence which will be discovered by science and medicine (Fisher, 1923; Dublin, 1942). The basic elements of normal life, such as proper hygiene and nutrition, are most probably still very far from ideal, in spite of the truly remarkable progress in these fields of physiology and medicine.

Moreover, senescence is complicated and accelerated by those pathological features and diseases which are not necessarily associated with normal old age, since they are not present even in some rare cases of less-pronounced pathological ageing (for example, senile mental deterioration, effects of improper nutrition, accumulation of and auto-intoxication with metabolic products, gastro-intestinal auto-intoxication, hypertension, arteriosclerosis, and certain disorders in the functioning of the heart, liver, kidneys, and glands of internal secretion). Hirsch (1945) shows this fact clearly for arteriosclerosis in one of his careful investigations dealing with the relation of this disease to the processes of ageing.

There are several promising lines of research concerning pathological senility, but only two examples will be mentioned.

1. *Auto-intoxication with Metabolic Waste Products.*—Some results of primary importance have been obtained with tissue cultures in the brilliant experiments of Carrel and his co-workers (1921, 1922, 1937), extended and supplemented by Cohn and Murray (1925), Hoffman *et al.* (1937), Goldschmidt *et al.* (1937), Medawar (1940), and others, and well summarized by Medawar (1946). In cells isolated from the organism and living *in vitro* as a tissue culture senescence and death could be greatly postponed ("indefinitely" as suggested by Carrel, 1937, p. 4) if the metabolic waste products were not allowed to accumulate. In such conditions the "old" cells (i.e., those from older animals) have just as high a capacity of growth as young ones. The old cells merely take a longer time than do the young ones in starting their growth. Professor Pearl (1922), similarly to Carrel, concludes that (p. 75) "senescence appears not to be a primary attribute to the physiological economy of cells as such," and (p. 67) "that the individual cells and tissues of the body, in and by themselves, are potentially immortal."

In connexion with these experiments *in vitro*, Carrel performed a striking although drastic experiment *in vivo*. The experiment has been described by one of his co-workers (Du Nouy, 1936). At the Rockefeller Institute there was a dog nearly 18 years old. The animal never stirred from its corner and could hardly get up to eat. It slept all day, its coat was coming out, its eyes were dim, and the eyelids were stuck together. Nearly two-thirds of its blood was removed, the red cells centrifuged, washed in Ringer solution, then mixed with fresh Ringer solution so as to re-establish the initial volume of the blood and reinjected into the dog. After recuperation the operation was repeated. After the second operation the dog not only lived but, when completely recovered, was quite different: it ran and barked, became lively and active—in particular, sexually active—its lids cleared, and its fur started to grow again. Although such a relief could be of a temporary character only, and the actual operation could not be considered for human geriatrical research, the significance of the experiment is considerable.

2. *Nutritional Experiments.*—The experiments of Sherman and others (1937, 1939) and McCay (1942) and their co-workers suggest another promising line of gerontological research. They were able to obtain prolongation of the life-span and improvement of the health of rats either by adding an extra amount of vitamins and calcium to a diet already adequate in all respects (Sherman) or by quantitatively restricting such a diet (McCay). Carrel (1937) in experiments on mice obtained results similar to those of McCay.

Of course, the results of experiments on animals do not necessarily mean that the same effects will be obtained on human beings. Research on animals, however, must precede geriatrical trials on human beings. Experiments on such short-lived animals as rats and mice give hope for a comparatively more rapid success in obtaining normal individuals with physiological senescence than do clinical trials on human beings. Moreover, attempts to change a pathological senility into a physiological one may perhaps bring about considerable changes in the human organism. This indicates the

possibility of grave danger, perhaps fatal, and necessitates therefore the greatest caution, and only by preliminary research on animals can we ensure absence of dangerous effects. It must also be emphasized that in research on gerontology the study of pathological senescence is as important as that of physiological ageing.

Definition of Old Age, and Tests for the Process of Ageing

At present, gerontologists must unavoidably be satisfied with a definition which disregards the most fundamental fact—namely, that we do not know the causes, features, and standards of normal physiological senescence. It can be expressed only in terms of the processes (effects) of ageing as we can observe them now. Because of this, until our knowledge of the subject is more complete such a definition can only be of a temporary character. Moreover, this definition should be based on facts which have been studied with reasonable accuracy.

From the point of view of these requirements the best definition of ageing has been given by Professor Warthin (1929, p. 74). He constructs it on pathological and clinical observations which have been obtained by all the investigators of the subject; namely, it is agreed that hypoplasia, or atrophy of organs, is one of the most important and typical changes and features of ageing. Hence Warthin defines ageing as a "major involution" of the living organism, of all its organs, tissues, and functions. Since all of them are correlated with and dependent on each other, the involution of each single organ, "once well initiated, may through the weakening or loss of the given function initiate or strengthen retrogressive changes in other organs. The various lines of involution are not wholly independent, but, in the general economy of the organism, aid and supplement one another until various vicious circles and correlations of retrogression are produced." Although this definition deals only with the simplest factual effects of ageing, it is very helpful in indicating various urgent schemes of gerontological research.

In the first place, a detailed investigation of hypoplastic and atrophic changes in the organs and tissues is very important, especially in the earliest latent form of relative hypoplasia as measured by changes in weight or linear measurements of organs and cells. The first results of such research were based on the data independently obtained in two American laboratories (Donaldson, 1924; Freudenberger and Billiter, 1935; Freudenberger and Clausen, 1937a, 1937b; Freudenberger and Hashimoto, 1937, 1939; Freudenberger and Howard, 1937) and in the Oxford Gerontological Research Unit (Korenchevsky, 1942, 1948; Korenchevsky and Jones, 1946, 1947, 1948). These data are in complete agreement and show that the relative decrease in weight of organs (relative involution) can be used as one of the tests for and indications of ageing in rats. Most probably this test will be reliable also for human material, as shown by investigations and recalculations (Korenchevsky, 1942) of the data so far available.

The test appears to be not only as good as many other tests of ageing but of great importance because it deals with one of the main changes and features both of ageing and of old age. It has to be supplemented, however, at least by histological examination.

At present, however, every test or indicator of ageing is handicapped by two difficulties. First, it is not known whether our tests will be valid for the processes of normal physiological senescence. Secondly, practically no feature of present-day senescence can be regarded as specific for old age only. Any of them might be present in or after some diseases, or occur in the changes produced by mental or physical stress and duress, or develop in or after some other pathological conditions. For example, in some rare cases the hair does not become grey in old age, whilst in some young ones it becomes grey in a very short time under the stress of an emotional crisis. In young rats certain vitamin deficiencies produce greying of fur (Unna *et al.*, 1941; Ansbacher, 1941; Ralli and Graef, 1943), atrophic skin (Morgan and Simms, 1939), and osteoporosis (Korenchevsky, 1922). Baldness might start to develop at an early age, or (Hamilton, 1942) can be produced by suitable doses of androgens.

A premature appearance of senile wrinkled skin was observed and described by Merschejewsky (1876), Pelikan (1876), Pittard (1934), and Tandler and Grosz (1913) in castrated men. Arteriosclerosis, hypertension, senile kidneys, senile heart, etc., might be almost absent in some cases of senescence. For instance, Hirsch (1945) did not find any signs of arteriosclerosis in 9.5% of autopsies in 400 old men aged more than 65 and examined by him.

From all the above-mentioned facts it follows that in present-day gerontological research a correct understanding and an accurate definition of the processes of ageing, or of the anti-ageing properties of any factor examined, could be obtained only after performance of several morphological, physiological, and biochemical investigations, both experimental and clinical (Korenchevsky, 1948). Since such a manifold investigation is technically impossible for a single research worker, the conclusions which he makes have to be drawn with reservations as judged by the test (or tests) of ageing applied in the experiments performed.

Causes of Ageing

So far we do not know the *main primary causes* of ageing, nor are we able to begin investigation of them before cases of normal physiological senescence are available. Heredity, according to some research workers (e.g., Pearl, 1922, 1931; Pearl and de Witt Pearl, 1934), influences longevity. If this is so, future research might discover a hereditary factor which has a connexion with the primary causes of ageing. Dublin and Marks (1942), however, emphasize difficulties of such research in man: "There may be strong beneficial influences from survivorship of parents on longevity of offspring . . . and these influences may have nothing whatever to do with heredity."

Professor Child (1915), one of the first gerontologists to have a sharp insight into and clear understanding of the problems of ageing, concludes in these words in dealing with the importance of heredity for geriatrical research (p. 310): "The advance of knowledge and of experimental technique may make it possible at some future time to bring about a greater degree of rejuvenescence and retardation of senescence in man and the higher animals than is now possible, but when we remember that the present condition of the protoplasmic substratum of these organisms is the result of millions of years of evolutionary equilibration we cannot but admit that this task may prove to be one of considerable difficulty."

In the case of the *secondary causes of ageing* the possibilities for gerontological research are more satisfactory. These causes should be defined as non-specific but capable only of hastening the process of ageing. A great number of the secondary causes might include any of those non-specific factors which increase "wear and tear" and involution, general or only of one or more organs or tissues. They *accelerate* the main process of ageing, chiefly by producing "secondary vicious circles of ageing" (Warthin).

Infectious diseases, intoxications, deficiencies of vitamins or hormones or any other vital factor, any pathological changes in any tissue, organ, or blood vessels, physical or mental traumas, etc., might belong to this category. For example, hypothyroidism might produce a number of features of senility, even (Hertoghe, 1899) in the form of mild deficiency. Castrated men often develop some senile changes prematurely (Merschejewsky, 1876; Korsakow, 1898; Pittard, 1934), although they might preserve their mental faculties. Thus Korsakow writes (p. 340): "The eunuchs are ageing early, at the age of 40 producing an impression of 60-year-old men." Professor Pittard (p. 327) records: "The men castrated after puberty appear to age very rapidly, as also their congeneric fellows do, who have been castrated early. They become prematurely wrinkled and acquire soon the appearance of old women." In a patient with diphtheria the toxin producing degenerative changes in the heart accelerates its ageing, but obviously this is not one of the primary causes of physiological senile changes in that organ.

It is obviously illogical, however, to expect (as some authors do) that a secondary cause can *produce the whole* complex of ageing in all organs, tissues, and their functions when this cause is able to accelerate sometimes only a single process of senescence in one organ or tissue. Moreover, the secondary causes of senescence, not being the primary causes of ageing, produce chiefly their own primary action according to their functional nature (for example, effects specific for each

hormone or vitamin, or their deficiency). This action, although accelerating senile change or changes in some organs, in one or two other organs simultaneously might produce an effect which is typical of the specific function only but not of senility (e.g., a delay in thymus involution and, in male rats, adrenal hypertrophy after castration). It is an urgent task to investigate all these secondary causes and their vicious circles in order to illuminate their possible role in the senility complex and to understand how to break these vicious circles for geriatrical purposes. From this point of view investigation of endocrine organs is specially important.

In the Oxford Gerontological Research Unit (Korenchevsky and Jones, 1946, 1947, 1948) an approach to this problem gave some significant results. Changes in the relative weights, and histological examination, showed that in female rats ovariectomy accelerates, and the combination of sex and thyroid hormones reverse more or less completely, the relative involution in the organs investigated. It was, however, strongly emphasized that in these experiments, as in any other research on ageing, the gerontological interpretation of the results obtained is impossible without manifold morphological, physiological, and biochemical experiments (Korenchevsky, 1948). It is obvious that ovariectomy might belong only to the group of secondary causes of ageing and therefore alone could never produce the whole syndrome of ageing, nor, for the same reasons, could hormones reverse this syndrome.

Moreover, since the action of the secondary causes, in particular that of ovariectomy, is not specifically ageing, and since the hormones might belong to the secondary reverse factors only—i.e., non-specific ones—discrepancies between the changes produced by them and the ageing or anti-ageing effects respectively are always possible. For example, androgens increase the involution of adrenals, whilst exerting an anti-involutionary effect on other organs investigated; ovariectomy at the beginning delays the involution of the thymus, but accelerates that process in some other organs. The clear predominance and importance of the special effects decide the gerontological significance of the factor concerned.

Summary

Gerontological research is handicapped by the basic difficulties of the problem; the span of life and the process of ageing are abnormal, and therefore the normal standard features and the primary causes of physiological senescence and old age are unknown.

It is possible, however, to investigate the secondary causes of ageing and pathological senescence as observed at present. This research is as important to gerontology as is that on physiological old age.

A definition of the secondary causes of ageing is given and the value of the present-day tests for ageing is discussed.

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MEDICAL NEW YEAR HONOURS

The names of the following members of the medical profession were included in a New Year Honours List published in the *London Gazette* on Jan. 1.

Baron

Sir JOHN BOYD ORR, D.S.O., *M.C.*, M.D., D.Sc., LL.D., F.R.S. Lately Director-General of the Food and Agriculture Organization of the United Nations.

Privy Councillor

EDITH CLARA SUMMERSKILL, M.R.C.S., L.R.C.P., M.P. Member of Parliament for West Fulham since 1938. Parliamentary Secretary, Ministry of Food, since 1945.

G.B.E. (Civil Division)

Sir WILLIAM WILSON JAMESON, K.C.B., M.D., F.R.C.P. Honorary Physician to the King. Chief Medical Officer, Ministry of Health and Ministry of Education.

K.C.V.O.

Sir WILLIAM GILLIATT, C.V.O., M.D., M.S., F.R.C.P., F.R.C.S. President of the Royal College of Obstetricians and Gynaecologists.

Knighthood

HENRY COHEN, M.D., F.R.C.P. Professor of Medicine in the University of Liverpool.

HUGH ERNEST GRIFFITHS, C.B.E., M.S., F.R.C.S., Surgeon, Albert Dock Hospital, London, E. For services in the industrial rehabilitation of disabled persons.

SYDNEY ALFRED SMITH, C.B.E., M.D., F.R.C.P.Ed. Regius Professor of Forensic Medicine and Dean of the Faculty of Medicine in the University of Edinburgh.

C.B. (Military Division)

FREDERICK HARRIS, C.B.E., *M.C.*, M.B., B.Ch., late Royal Army Medical Corps. Honorary Surgeon to the King.

LIONEL FREDERICK STRUGNELL, M.B., B.S. Surgeon Rear-Admiral, Royal Navy. Honorary Physician to the King.

C.M.G.

ARTHUR BARTON PILGRIM AMIES, D.D.Sc., F.R.A.C.S., F.A.C.D., D.L.O. Professor of Dental Science in the University of Melbourne.

THOMAS AITKEN AUSTIN, L.R.C.P.&S.I., D.P.H., D.T.M., D.T.H. Colonial Medical Service. Director of Medical Services, Uganda.

RICHARD BRUNEL HAWES, M.B., B.S., F.R.C.P., D.T.M.&H. Consulting Physician to the Colonial Office.

MONTAGU TRAVERS MORGAN, *M.C.*, M.D., D.P.H. Medical Officer of Health, Port of London. Medical Adviser, Ministry of Transport.

C.B.E. (Military Division)

ROBERT WALSH MUSSEN, M.D., M.R.C.P. Surgeon Captain, Royal Navy.

C.B.E. (Civil Division)

WILLIAM ARTHUR BULLOUGH, M.Sc., M.B., Ch.B., D.P.H. County Medical Officer for Essex.

JOHN BURTON CLELAND, M.D., Ch.M. Formerly Professor of Pathology in the University of Adelaide.

EMILY HANCOCK MCKINNON, M.B., B.Ch., of Dunedin, New Zealand. For services in the field of medicine and welfare of women.

NORMAN MANSON, M.B., Ch.B., D.O.M.S. Warden, Hospital of St. John, Jerusalem.

WILLIAM BENTLEY PURCHASE, *M.C.*, M.B., D.P.H. H.M. Coroner for the Northern District of London.

WILLIAM ROBERTS, M.D., F.R.C.S. Medical Superintendent, Grace Hospital, Newfoundland.

O.B.E. (Military Division)

STEPHEN MACKENZIE, M.R.C.S., L.R.C.P., D.C.H. Lieutenant-Colonel (temporary) (now Major), Royal Army Medical Corps.

SIDNEY RICHARD CARLYLE NELSON, M.D., M.C.P.&S. Wing Commander, Royal Air Force.

O.B.E. (Civil Division)

MRS. MARGARET MARY BASHAM, M.B., Ch.B., D.P.H. County Director, Monmouthshire Branch, British Red Cross Society.

GEORGE FREDERICK BAXTER, M.R.C.S., L.R.C.P. Senior Surgeon, Public Hospital, Kingston, Jamaica.

ERIC HATTAWAY BRIDGMAN, M.B., B.Ch. Superintendent, Rotorua Hospital, New Zealand.

JOHN CHARLES JOSEPH CALLANAN, M.D. Director of Medical Services, Swaziland.

CHARLOTTE ANN DOUGLAS, M.D., F.R.C.O.G., D.P.H. Medical Officer, Department of Health for Scotland.

CYRIL FRANCIS FERNANDO, M.D., M.R.C.P. Medical Officer and Physician, General Hospital, Colombo, Ceylon.

GEORGE GIGLIOLI, M.D., M.R.C.P., D.T.M.&H. Honorary Government Malariologist, British Guiana.

RICHARD MURCHISON MORRIS, M.D., D.P.H., D.T.M.&H., Medical Director and Secretary for Health, Bulawayo, Southern Rhodesia.

HAROLD BURNET PORTEOUS, M.B., Ch.B. Wing Commander (ret.), Royal Air Force. Medical Officer, Board of Customs and Excise.

ERNEST ALBERT HAROLD RUSSELL, M.B., B.S. Honorary Consulting Obstetrician, Queen Victoria Maternity Hospital, State of South Australia.

Hon. O.B.E. (Civil Division)

FRANCIS AKANU IBIAM, M.B., Ch.B. Medical practitioner on the staff of the Church of Scotland Mission, Nigeria.

LOUBE MARY-MADELEINE LENGAUER. Medical Officer, Leprosy Control, Nigeria.

M.B.E. (Civil Division)

Mrs. OLGA KONSTANTINOVNA ABBOTT. Physician, Ethiopian Vice-Ministry of Health, Addis Ababa.

CHARLES EDWARD ETHERIDGE, M.B. Admiralty Surgeon and Agent, Whitstable, Kent.

JOSEPH GALEA, M.D., D.P.H. Medical Officer of Health, Malta.

Mr. GEORGE NORTH, *M.C.*, LL.D., the Registrar-General, was appointed C.B., and Mr. G. R. EDWARDS, the secretary of the Royal Society of Medicine, an O.B.E.

THE KING'S HEALTH

The following bulletin was issued from Buckingham Palace on Jan. 3:

Since the bulletin of Dec. 13, 1948, the King has made uninterrupted progress. His general health is entirely satisfactory. On both right and left sides the arterial circulation in the legs and feet is improving slowly. It is not yet sufficient to allow more than strictly limited activity when his Majesty leaves London to continue his convalescence in the country.

MAURICE CASSIDY. J. PATERSON ROSS.
THOMAS DUNHILL. MORTON SMART.
HORACE EVANS. JOHN WEIR.
J. R. LEARMONTH.

The bulletin is the fifth to be issued and the first which has been signed by Dr. Horace Evans, who has been physician to Queen Mary since 1946.

Nova et Vetera

ARE FEMALES BORN CO-TWIN WITH MALES STERILE?

"It is a popular opinion, and I do not know any instance to discountenance it, that if twins be of different sexes, the female is sterile."

Your inquirer (*Journal*, Nov. 13, p. 887) may be interested in a work by Sir James Young Simpson* in which these words (taken from an obstetrical publication dated 1843) form the opening sentence. Famous as the first man to use anaesthesia in childbirth, Simpson has many other claims to undying fame; and during his short but intensely active life he poured forth a seemingly endless stream of writings covering an amazing variety of medical and scientific subjects. This article is typical of his style, and, although it is now a hundred years old, extracts from it may interest present-day readers.

Having, as was his wont, arrested his reader's attention by an apt quotation, Simpson plunges without ado into his discourse. First he deals with comparative physiology. From John Hunter (1779) he quotes:

"When among black cattle, the cow brings forth a male and a female at the same birth, the male is a perfect bull-calf, but the apparent female is almost always imperfect in its sexual organization. Female cattle of this kind, born co-twin with males, have long been distinguished in this country under the name of free-martins. In external appearance and form of body they usually resemble the ox and spayed heifer more than either the entire male or the entire female of the species. They commonly grow to a larger size than either the bull or the cow, and have horns like those of an ox, and a tone of bellowing similar to his, with the same marked disposition to become fat under the use of nourishing food. In general they do not show any sexual desire for the bull, or the bull for them."

Hunter's dissections showed that the external sexual organs were of the female type but that the vaginal canal was contracted in its upper part, and the internal female organs, the uterus, Fallopian tubes, and ovaries, were "altogether rudimentary and imperfect in their structure." After reference to other authorities, Simpson records his own examination of freemartins "killed in the shambles of this city" and tells how he "found all of them formed after the imperfect and abnormal type pointed out by Mr. Hunter." He continues:

"The butchers in Edinburgh and its neighbourhood, of a number of whom I have made enquiries upon the subject, seem to be perfectly familiar with the fact, that in the free-martin, whose flesh they usually reckon of a superior quality, the womb, or calf-bed, as they term it, is in almost all cases apparently wanting; and all our intelligent agriculturalists in the Lothians are acquainted with the sterile character of these animals."

Characteristically, Simpson now turns to the examination of old Roman writings. He finds reference to the existence of sterile cows ("*taurae*"), which were set aside and trained to the plough; and he speculates on whether these animals were, in fact, freemartins.

Next he indicates the complexity of the subject. He recounts cases in which, despite the circumstances of its birth, the female calf of dissimilarly sexed twins had, when grown, full reproductive abilities. He states that he had been unable to find any evidence of the occurrence of a freemartin in sheep or other animals which are normally uniparous but occasionally produce opposite-sexed twins:

"I have hitherto been equally unsuccessful in tracing out any instance of a twin mare or she-ass, born under the circumstances already pointed out, being reared to maturity. The mare, indeed, appears only in extremely rare cases to produce twins, and these . . . seldom survive for any length of time after birth."

Turning now to the human species, he states:

"A prejudice in reference to the infecundity of human females born co-twin with males exists to a considerable extent amongst the peasantry of the Lothians, and has very probably been derived from the analogy of the free-martin cow."

He abruptly forces the importance of this matter on the reader's attention by the quotation:

"The mischief to which the opinion might give rise, in causing a girl to be rejected as a wife for a defect, or taken for an excellence, according to sterility might be regarded, which she did not possess, is incalculable."

He next presents records from Edinburgh, Dublin, and London hospitals to show the frequency of dissimilarly sexed twins and states that, contrary to current opinion, it was "by no means uncommon"; one case occurred in every 199 labours.

Simpson now turns to his main theme. He presents numerous records of cases in which the female of dissimilarly sexed human twins did in fact have issue. Included in these is a case of plural pregnancy, occurring in 1827, in which a female infant, co-quadruplet to three males, became herself in the course of time the mother of triplets. Of 123 females born co-twin with males he discovered that no fewer than 112 had families, and that only 11 were without issue although married for several years. He concludes that "females born under the circumstances we are considering were *unproductive in the proportion of 1 in 10*."

Before drawing conclusions from these figures Simpson wisely turns his attention to the proportion of unproductive marriages in the society in general—a subject on which there was at that time no available information. He had the records of two large self-contained villages examined—Grangemouth and Bathgate—"one community chiefly of a sea-faring population,

**Selected Obstetrical and Gynaecological Works of Sir J. Y. Simpson*, ed. by J. Watt Black, p. 822. Edinburgh, 1871.

and the other of persons engaged in agriculture and manufacture." From these figures he concludes that, allowing for couples not yet married for five years, *one marriage in ten was without issue*. With admirable resource he "extended the basis of data" by examining the histories of marriages contained in a work on the "British Peerage" for 1833. In this case the proportion of barren marriages was, he found, 1 in 6$\frac{1}{2}$.

Simpson could now "form a just conclusion" that females born co-twin with males were at least as productive as females in general. He adds that error, if any was present, was in the direction of over-estimating the number of barren marriages in these females:

"In relation to such a question as the present, all minds are too liable to be impressed with and recollect instances illustrative of the supposed rule and common opinion, whilst the apparent exceptions to it are unattended to or forgotten."

Further, Simpson found that the fruitfulness of these women was not impaired. The average number of children born to each mother was 4$\frac{8}{10}$; while in the control group (this modern technical term is not used by Simpson!) the corresponding number was 4$\frac{3}{10}$.

"The whole enquiry," he observes, "forms an apt illustration of an old remark, that in Medicine it often requires a much greater extent of observation and research to disprove satisfactorily an alleged and accredited fact, than was ever expended, either upon the original development or subsequent confirmation of it. In the present instance, the results have turned out to be perfectly contradictory to the opinion which I, in common with others, held regarding the infecundity of the female in double-sexed twins, when I commenced looking into the subject; and instead of finding my preconceived ideas confirmed by the investigation, they have, on the other hand, been completely confuted by it."

Finally, Simpson expresses great surprise at the phenomenon of the freemartin:

"For certainly it cannot but be considered as an extraordinary circumstance, that, in the cow, the twin existence in utero of a male along with a female should, as a general principle, lead to so great a degree of malformation . . . in the sexual organs, and in the sexual organs only . . . and be limited entirely to the reproductive organs of the female twin, while those of the male twin are perfectly and fully developed. . . . The whole series of circumstances, when considered in conjunction with each other, seems to form, in relation to the origin of malformations, one of the strangest and most inexplicable facts to be met with in the study of abnormal development."

Can we wonder at Simpson's amazement? No explanation, no glimmer of understanding, was possible. Knowledge of "chemical messengers" in the blood stream was more than half a century ahead.

As an example of a perfectly constructed paper, written in clear and arresting English, this publication of Simpson's must be hard to match. And how strange it is that the false belief he so clearly exposed and so forcefully dispelled should to this day linger on in some parts of our country!

J. CHASSAR MOIR.

Reports of Societies

CHELSEA CLINICAL SOCIETY

The third dinner meeting of the session was held on Dec. 14 at the South Kensington Hotel, S.W.7, with the president, Mr. Nils Eckhoff, in the chair. A most interesting discussion on "Films and their Influence" was opened by Mr. Sidney Gilliatt, of the J. Arthur Rank Organization, and Mr. Noel Langley. A sound film showing cinematic technique from its inception was also exhibited. The discussion was continued by Drs. Stewart Webb, Seth Smith, Keane, Eckenstein, Chadwick, McCormick, Guy Daynes, Skene Keith, Guy Beauchamp, Mr. Havelock Allen, Mr. Cutler, and Judge Norman Daynes. Mr. Gilliatt and Mr. Langley replied.

The Ministry of Transport has issued Amendment No. 3 to *The Ship Captain's Medical Guide, 1946*. It advocates "paludrine" as the best prophylactic against malaria, and states that this drug will in future replace mepacrine in the Ship's Medical Scales. Copies of the Amendment are obtainable from H.M. Stationery Office or through any bookseller for 3d.

Correspondence

Malaya Branch of B.M.A. and R.M.B.F.

SIR,—You recently published (Nov. 13, 1948, p. 875) a letter from me expressing the thanks of the Royal Medical Benevolent Fund for gift parcels for the beneficiaries of the Fund sent by members of the B.M.A. in New South Wales. It is now my pleasant duty to inform your readers that gift parcels have also been sent by your members in Malaya. The recipients have been deeply touched by the kind thought of these colleagues far away when the donors themselves can hardly be living in a bed of roses at the present time. I send a message of heartfelt thanks to you, Sir, in the hope that it will thus reach all those who have shown such kindness and generosity.—I am, etc.,

WEBB-JOHNSON,
President,
Royal Medical Benevolent Fund.

Whither Tuberculosis?

SIR,—I was most interested to read Dr. G. Lissant Cox's letter (Dec. 25, 1948, p. 1118), as I myself have been concerned about certain trends discernible in the plans which are being outlined for the new regional chest services. It seems to me that some serious mistakes are about to be made. Dr. Cox suggests that if the chest physician or tuberculosis officer becomes too "clinical" he is in danger of losing his soul, and, although this is probably an overstatement, yet Dr. Cox is right in essentials and as usual has put his finger on the most important point at issue.

In the past I have always advocated that as far as possible chest clinics should be sited in the out-patient departments of general hospitals not only in order to rescue the T.O. from his isolation and to subject him to stimulation by the contact with and criticism of his fellow physicians, but also so that these physicians should come to understand something of the work that goes on in a chest clinic and see perhaps for the first time what real environmental medicine is. For it is in the environmental field that the old tuberculosis service did such great pioneer work. I had not foreseen, however, that with the acceptance of this principle the chest physician would be tempted to devote himself exclusively to clinical work and to desert the task which previously he had on the whole done very well. Yet this is precisely what is going to happen unless a stand is made. Chest physicians are demanding beds in sanatoria where they can treat their patients and "see them right through," as they say, and sanatorium physicians are asking for a share of the clinic work. Such a policy has a superficial attraction but it ignores the realities of the problem.

The treatment of phthisis from activity to quiescence is a very complicated business, requiring experience, patience, and skill. A pneumothorax is easy to induce, but its complications are numerous and, in unaccustomed hands, frequent. Many a patient would have lived a great deal longer if it were as difficult to do a pneumothorax as to do a thoracoplasty. Furthermore, therapy is becoming even more complicated by the introduction of specific drugs. I feel, therefore, that sanatorium physicians have a task before them which should exercise all their skill. The chest physician's job on the other hand is quite different, requiring a different sort of person. He has on the clinical side a wide field of differential diagnosis (for tuberculosis can simulate most other diseases) and minor therapy. His clinical ability must be no less than that of the sanatorium physician, for the assessment of the present condition and probable trend of an individual case requires skill and understanding which can only be acquired by experience in all branches of tuberculosis work. The exercise of clinical judgment only in diagnosis and assessment should not deter the man of the right temperament from this job, for it has compensations in the sphere of human relations. He has to do with management, aftercare, rehabilitation, and above all prevention. This latter covers such matters as sociology, psychology, and non-party politics, and will soon include the use of B.C.G.

It is on the field of prevention that the battle against tuberculosis will be won, as with so many diseases in the past, while

in the sanatorium beds the individual casualties will be treated. Thus the chest physician's job can be one of the most satisfying in medicine. He should regard it as a reproach to his work if a patient is found in his area with bilateral phthisis. He should be ashamed of it and inquire closely how it came about. All his new cases should be minimal. It may even be that with improvements in bacteriological technique a new horizon of diagnosis is in sight, that in the future our patients will be x-ray negative and T.B.-positive, and that with proper management and advice we shall be able to prevent the onset of radiological phthisis. This may seem at present an impossible vision, but no one can deny that the outlook in the tuberculosis world has become immeasurably wider and clearer in the last ten years. With these considerations in mind and many others too numerous for a short letter, the task of the chest physician should be seen as one which gives both intellectual and emotional satisfaction. It would indeed be an exceptional man who could do it well and at the same time conduct good clinical therapy.—I am, etc.,

Aylesbury, Bucks. STEPHEN HALL.

Rheumatoid Arthritis and Ruptured Tendons

SIR,—I have read with interest the paper by Dr. G. D. Kersley (Nov. 27, 1948, p. 942) and Dr. Peter London's letter (Dec. 11, 1948, p. 1039) on ruptured tendons in patients with rheumatoid arthritis. Early this term my attention was drawn to the condition found in certain shoulder-joints in the dissecting room. Out of 22 joints examined 10 showed some sign of arthritic change, and in 6 there were gross changes. In these 6 specimens the long head of the biceps tendon was fixed to the bicipital groove in the region of the surgical neck of the humerus. Judging by the atrophic belly of the muscle, I would say that the tendon had ruptured and become secondarily attached to the humerus. It would seem that the condition is much more common than has been previously reported, and I am arranging for a search to be made regularly in dissecting-room material. —I am, etc.,

Department of Anatomy, University College, London, W.1. J. T. AITKEN.

Fibrositis

SIR,—In the letter by Dr. T. Blanchard Sellors (Dec. 18, 1948, p. 1082) I would humbly submit it is indeed a remarkable pathology that accounts for his interpretation of the word "fibrositis." I am not aware that there is as yet an agreed definition of this vexed word, and I think it is because there are so many individual interpretations of it that there is so much misunderstanding. This is clearly illustrated in the many letters appearing in the *Journal* since Dr. James Cyriax put forward his controversial yet masterly attempt (July 31, 1948, p. 251) to clarify the issue. It is to be hoped that doctors will soon agree on some definite terminology.

That the symptoms of fibrositis coming on for no apparent reason are all in fact "the result of articular lesions" is well illustrated by the following chance occurrence. A man aged 56 complained of a painful and stiff neck. It had come on gradually during the last week, but when seen his head was flexed and he was unable to look up above the horizontal. On questioning, he said he had had pain and stiffness of his neck in 1943 and 1946. In 1946 he visited an osteopath, who "stretched" his neck so severely that he was much worse.

The examination was instructive. The head was held stiff and was moved most cautiously. All movements were limited, but especially side flexion both to the left and right and rotation of the chin to the left. Passive movements were only slightly increased, being limited by pain. Resisted movements caused notably no pain. On palpation there was marked tenderness on the right postero-lateral aspect of the neck, mostly localized opposite C2–C3, slight tenderness between spinous processes C2–C4, and much tenderness at the occipital insertion of the right trapezius and semispinalis capitis muscles. The left trapezius (upper outer border) was very tender. Shoulder and elbow-joint movements were free.

A course of radiant heat and massage was arranged the same day, as he had found it of benefit before. However, the following day he phoned the masseuse asking her not to come, as when he woke up that morning he found he could look around naturally, move his head freely in all directions, and was quite free from pain. On examination later this was confirmed. A truly remarkable "fibrositis."

The diagnosis was that of derangement of a cervical intervertebral joint, C5–C6 or C6–C7, osteoarthritis with loose-body formation in a man of this age being very common. Reduction or replacement of the loose body had occurred naturally. Confirmation of this diagnosis was presented in a letter from the patient's previous doctor, who reported as follows: 1942, lumbago and sciatica; 1942, severe fibrositis of neck; 1943, coccygodynia; 1943, neuritis of left arm, secondary to stiff neck; 1946, right suprascapular fibrositis; 1946, some anaesthesia of left forearm.

It is interesting to note the combined cervical and lumbar disk lesion, which is so frequent an occurrence, and to observe the value of manipulation in such lesions.[1]—I am, etc.,

Ryde, Isle of Wight. TREVAN HAMBLY.

REFERENCE

1 Cyriax, J., *Rheumatism and Soft Tissue Injuries*, 1947, London.

"Comedomastitis"

SIR,—For some time I have been puzzled by two cases of "chronic mastitis" which did not fit into the usual description of this disease.

The first case I saw at the Metropolitan Hospital three years ago, when a married woman of 50 presented herself with what appeared clinically to be a scirrhous carcinoma of the breast. It was not until after radical mastectomy that the tumour was sectioned and the breast revealed caseous debris in the large ducts and a cyst which was filled with similar grumous material. The pathologist reported that there was no evidence of malignancy in the portion of the breast and that the condition was one of chronic cystic mastitis; he remarked that the ducts and cysts were filled with milk-like debris.

The second case occurred in private practice last year, and was in a single woman of 38 who had multiple smooth swellings in both breasts. Clinically there was no evidence of malignancy, and chronic cystic mastitis was diagnosed. A biopsy was performed in order to reassure the patient that the condition was not malignant, and it was found that a thick grey material could be squeezed from the large ducts like toothpaste out of a tube. The pathologist reported that microscopic section showed chronic cystic mastitis, but he noted that several of the larger cysts were filled with milk-like debris resembling a galactocele.

I could find no reference in the literature to a description of this condition. Sampson Handley mentioned duct catarrh, where plugs of epithelial debris blocked up the ducts, and Cheatle had noted dilated ducts with retained secretion in carcinomatous breasts. Tice, Dockerty, and Harrington[1] have recently given a full acoount of this condition under the name of "comedomastitis." They state that:

"Comedomastitis is a disease of the breast characterized by dilatation of the lactiferous ducts, which are distended with inspissated grumous material that may be expressed from the cut ends of the ducts much as comedones are expressed from ordinary blackheads. It is a disease of the large ducts, in contrast to chronic cystic mastitis, which is a disease of the acini and ductules. Marked clinical similarity to mammary malignancy may be present when comedomastitis results in an indurated area of the breast which is fixed to the skin and is associated with a retracted nipple."

There is little doubt that this condition is a definite pathological entity, although it is intimately related to chronic cystic mastitis; as Tice, Dockerty, and Harrington point out, time may prove that the two types are responses to different hormones and that comedomastitis is merely a phase in the constantly changing panorama of breast pathology.—I am, etc.,

El Alto Hospital, Peru. JOHN M. JACKSON.

REFERENCE

1 *Surg. Gynec. Obstet.*, 1948, **87**, 525.

Treatment of Infertile Marriage

SIR,—I disagree with the criticisms of Miss M. Moore White and Dr. E. Friedmann (Dec. 11, 1948, p. 1035) of Mr. Christie Brown's paper. They surely seem to have missed the main object of his article. Most people who deal with infertile marriage will agree with Meaker's[1] view that sterility often results from multiple causative factors. He further points out that any one of these factors is often insufficient in itself to prevent conception, whereas all of them combined are able to

depress the fertility level below the threshold for conception. On the other hand, the removal of one of these impediments will often result in a rise in the fertility level above the threshold for conception. This of course is the explanation why different procedures in the past have all had their zealous advocates.

Furthermore, many women seek advice on account of sterility but are unwilling to submit to special investigations. Mr. Christie Brown describes a simple plan which would appear to help a reasonable percentage, and it certainly warrants further trial in suitable cases. Miss Moore White and Dr. Friedmann also appeared to have overlooked that this simple plan was only advocated in cases where there was no clinical evidence of abnormality.

Mr. Christie Brown performs another useful service in stressing that the foetal environment is partly genetically controlled. In other words, the maternal capacity to retain the foetus depends on an adequate supply of hormones, which in turn depends on a healthy, well-developed chorion. The other factor, of course, is the capacity of the uterus to respond. Evidence and proof of the latter condition have now been produced, and a similar condition has been described in certain types of "anovulatory" menstruation. Proof of ovulation has been seen at laparotomy and normal hormone secretion shown by urinary assay, and yet the endometrium has not shown the usual response.

Without question, all the basic requisites for conception, production of ova and sperms, existence of an uninterrupted pathway, and a satisfactory nidation surface should ultimately be investigated, but surely there is no harm in trying this simple plan for some two or three months. Our object should be to achieve conception, and this does not necessarily include the cure of all the factors that are responsible for the infertility.—I am, etc.,

London, W.1. E. ROBERT REES.

REFERENCE

1 *Amer. J. Obstet. Gynec.*, 1930, **20**, 749.

Breast-feeding

SIR,—Dr. H. R. E. Wallis (Dec. 25, 1948, p. 1121) courteously supplies me with some American statistics in support of breast-feeding. What a pity it is that we should have to go to America for these as well as for our bread-and-butter. One sees clearly that more bottle-fed babies die in infancy from gastro-enteritis and pyloric stenosis, but surely this is inevitable, as most of them have had digestive troubles since birth. At least in most practices a baby is left at the breast till something goes wrong, and the weaklings go to the wall or rather to the bottle.

Your correspondent is not impressed by my four healthy bottle-fed children and the conviction, born of twenty-five years' observation in general practice, that the mythical benefits of breast-feeding are one great big fairy story. Let me quote my late partner, Dr. C. B. Hutchinson, who has five healthy bottle-fed children and over fifty years of similar experience. He assures me that he has never been able to determine any extra incidence of disease or lack of immunity in bottle-fed children during adolescence or later life, and he warmly supports my view that much unhappiness and maternal misery could be saved by early recourse to weaning. If our ideas are sound, as I sincerely believe they are, it is only fair to our present-day mothers that we should be able to speak comfortable words to them when they relinquish the almost impossible task of synthesizing wholesome milk from snoek, scraps, and sausage meat.

Nearly fifty years ago, when I survived bottle-feeding in the bad old days when only two or three indifferent baby foods were available, there was a very strong case for breast-feeding. In spite of this I have been blessed with personal health and vitality above the average. Now that such excellent baby foods are available at nominal prices I feel that the case for forced breast-feeding has collapsed and that we should, in fairness to our overworked young mothers, relieve them of this extra physical drain on the slightest pretext instead of starving their babies to breaking point. And I should like to be able to assure them with authority that they are in no way jeopardizing their baby's right to health and happiness in the future.—I am, etc.,

Walmer, Kent. JAMES S. HALL.

Perichondrium in Vascular Surgery

SIR,—As a plastic surgeon I have no experience of vascular surgery, but I have followed with interest all the great advances in the latter during the last few years. All plastic surgeons are interested in the reaction which occurs or the reception given to similar and dissimilar tissues when brought into contact with each other—this is the basis of successful grafting. In addition, a few years ago I did some research work on the subject, examining histologically the effects produced in rabbits' tissues by the introduction of a large number of substances. Perichondrium, when stripped from the costal cartilages, is tough and fairly strong, and has the property in an unusual degree of forming rapid adhesions to other tissues, promoting a local fibrosis and itself undergoing contraction. It would seem that these are properties which vascular surgeons are seeking in ligature material.

If sufficient perichondrium can be obtained for the case it would have the advantage of being living tissue, and would quickly form strong adhesions to the blood vessel concerned and to surrounding tissues; it would not be absorbed like catgut, nor produce necrosis like silk (if tied tightly), and, moreover, would tend to get tighter as it contracted. This contraction starts as soon as the perichondrium is free; therefore it should be removed only immediately before it is wanted. With the use of vitallium or acrylic tubes for uniting a divided artery it is admitted that the weak point is the ligature, as indeed it must be, for the free ends of the blood vessel beyond the silk ligatures must inevitably die if the ligature is tight enough, because of the destruction of the vasa vasorum. Whereas with fresh perichondrium new live cells grow and would unite the blood vessel and the ligature very quickly, and, moreover, instead of getting slack, it would get tighter.

I have used perichondrium chiefly for securing individual muscles of the face when they have by accident been avulsed from their attachments with the production of considerable disfigurement and disability—e.g., the orbicularis oculi. Strands of perichondrium used thus get a firm grip of the muscle and periosteum and promote adhesions most satisfactorily, and I do not know of any other substance, vital or non-vital, which will accomplish this purpose more than temporarily. Fascia lata is quite useless for the purpose; it has no adhesive or gripping properties, and a knot tied with it rapidly comes undone unless very carefully sutured.

As for the reasons for this adhesive reaction, it may be that more histamine is released by damaged perichondrium cells than by cells of other tissues, and that this produces a strong local reaction on contiguous tissues; or the clue may lie in the following sentence taken from Wells's *Chemical Pathology* (1925, p. 470): "Chondroitin is a gummy substance, which in turn may be split into acetic acid and a strong reducing substance, chondrosin. Chondro-sulphuric acid is the characteristic component of cartilage, but is also found in the walls of the aorta and other elastic structures." These suggestions are offered in the hope that by the pooling of experience some benefit may accrue.—I am, etc.,

Wellington, New Zealand. H. P. PICKERILL.

Millilitres Correct

SIR,—It is still the practice amongst manufacturers of medical requisites to state the dosage of their liquid preparations in cubic centimetres instead of the correct official millilitres. There may be laudable exceptions, but if so I have not come across them. One of the reasons which have been given to me for adherence to this incorrect nomenclature is that if millilitres were used many doctors would not understand them and uncertainty and confusion might result, especially when preparations were injected, since doctors generally use syringes marked in cubic centimetres.

I cannot believe that the millilitre is a strange and confusing measure to doctors; presumably they have used it from the beginning of their studies. Certainly all their measuring vessels are graduated in millilitres, and this unit, not the cubic centimetre, is official in the *British Pharmacopoeia*. Moreover, the enlightened policy of the *British Medical Journal* must by now have made the whole medical profession familiar with the millilitre. This being so, I do not think that a syringe marked in cubic centimetres would cause confusion, but nowadays such

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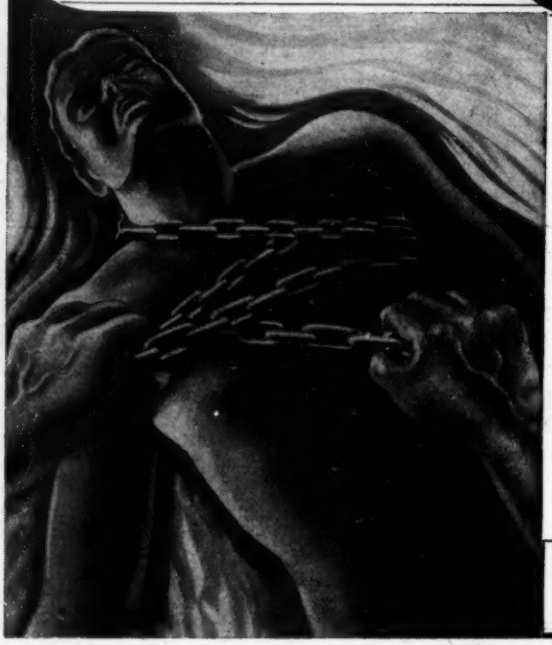

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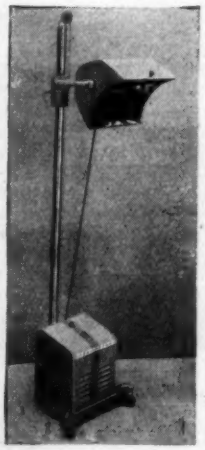

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a wrongly marked syringe is a reproach to the manufacturer. The British Standards Institution has issued a specification for syringes in which graduation in millilitres is prescribed, and makers should follow this prescription. I understand that syringes correctly marked in millilitres are now obtainable.

It is conceivable that many doctors, far from being perturbed by millilitres, may regard the statement of doses in cubic centimetres as indicating that manufacturers are behind the times and as evidence of ignorance or carelessness which may extend beyond the use of an incorrect unit of measurement. It seems to me that the adoption of the millilitre would be a "selling point" for manufacturers—evidence that they are up to date and correct in this and presumably in other matters relating to their business.—I am, etc.,

London, W.14. J. M. HAMILL.

Mineral Oils in Bread

SIR,—In a letter published in this *Journal* (Aug. 21, 1948, p. 401) under the heading "Liquid Paraffin in Baking" it was shown that the use of even highly refined mineral oil in quantity as an ingredient in cakes involved a potential hazard to health. This conclusion was based on microscopical examination of cake batters which revealed that minute droplets of mineral oil of particle size less than 0.5 μ persisted after baking. Evidence has been obtained by Frazer[1] that oil of such particle size can be directly absorbed through the intestinal wall and may lead to liver and other damage.

A detailed study of the potential distribution of mineral oils in bread has now been completed. Suggestions have been made to the baking industry regarding the use of such oils as tin-greasing agents and machinery lubricants, in which contact with dough may lead to some mineral oil absorption. It would appear that in view of the findings described later a clear distinction may be drawn between this form of use and incorporation of mineral oil in quantity as an ingredient in baked products.

The inherent dangers in the uncontrolled use of mineral oils have recently been reviewed[2–5] and their use as ingredients in foodstuffs condemned. These views are based on such evidence as interference with the absorption of carotene, vitamin D, calcium, phosphorus, and vitamin K, and the ability of mineral oil to destroy cells in the lymph nodes and to induce (when impure) tumours in rodents. In certain cases necropsies on human subjects known to have used mineral oil over a long period have shown the presence of oily deposits in the lymph nodes. It must be emphasized, however, that there appears to be no substantiated evidence of refined mineral oils producing carcinogenic effects on ingestion, and the experimental evidence on the heated oils is still inconclusive. It might be thought that as dough is baked in an oven at 450° F. (232° C.) there is some possibility of the formation of harmful oxidation products. This, however, is unlikely to occur, since the internal dough temperature is less than 212° F. (100° C.), and even at the point of contact between the dough and baking-tin oxidation will be slight in the atmosphere of carbon dioxide prevailing consequent on the fermentation conditions.

In view of the available medical evidence we have been guided in framing recommendations to the industry largely by the more clearly defined physiological defects which might accompany uncontrolled usage. These defects appear dependent on the oil being finely emulsified and absorbed through the intestinal wall. Alvarez[5] has shown that even after ingestion in the liquid form emulsification may subsequently occur, being effected by the bile salts, oleic acid, and glyceryl monostearate present in the bowel and acting as emulsifiers.

Microscopical examination of bread doughs containing mineral oil stained with scarlet red has shown that the degree of dispersion depends on the efficiency of admixing the oil with the dough. Emulsification of the oil with the water present in the dough does not occur, and the oil either is distributed as a thin film inside the dough when mixing is slight or, when thoroughly mixed, it forms a film apparently surrounding each starch particle and/or penetrates the gluten in the form of an unbroken macro-film. These latter conditions do not occur to any appreciable extent in baking practice. When oil is used to prevent dough adhering to the baking tin it forms a thin layer over the dough and is slightly absorbed during the baking. Observation of oiled bread doughs—baked in a micro-oven by the technique described in the above-mentioned letter—has shown no evidence of these films dispersing into droplet form. Thus it may be regarded that pure oil used as a grease or lubricant in bread production does not result in emulsion formation, and it is believed that subsequent emulsification in the bowel does not occur and that the chance of absorption through the intestinal wall is remote.

The difficulty of carbon tetrachloride extraction of the total mineral oil in breads and even pure starch "loaves" containing known quantities led us to the view that some of the oil was firmly bound to the crumb. A laboratory experiment was designed to copy somewhat the processes occurring when bread containing up to 2% mineral oil was ingested. Bread was boiled with 0.5N hydrochloric acid for a short time to imitate the breakdown caused by mastication, and the mixture was then rendered slightly acid and incubated at 38° C. for about 24 hours in the presence of the enzymes diastase and pancreatin to imitate the digestive process. It was found that the mineral oil still adhered to the residue resulting from this degradation and was little dispersed in the acid solution. This type of undigested residue might be compared with the roughage excreted from the human system. It is noteworthy that a parallel experiment in which glyceryl monostearate was added to the digest gave similar results.

It would appear, therefore, that mineral oils, when present in small amounts in bread, will not be liberated to any marked degree internally and that the possibility of emulsification and subsequent absorption is slight. Even this risk is eliminated should small residual quantities be metabolized, and evidence obtained with the paraffin deuterohexadecane[6] has indicated that such metabolism may well occur. The quantitative determination of mineral oil in bread will be described elsewhere. A survey of the quantity of mineral oil present in loaves purchased from 16 sources in Great Britain has indicated that the majority of bread examined falls within the recommendations suggested to the industry as a result of our investigations.

It has been suggested that bread should only contain mineral oil (1) if the quantity does not exceed 2,000 parts per million, and (2) if the chemical purity is not below that of liquid paraffin B.P. In these circumstances we believe that *pure* mineral oils may be safely used for the purposes specified in quantities not greatly exceeding 2,000 parts per million, as the chance of emulsification of oil in the bowel appears to be much smaller than with the same oil undiluted, and that at this level of usage the oil is probably largely excreted with the roughage, any residue being completely metabolized in the body.—We are, etc.,

The British Baking Industries Research Association, Chorleywood, Herts. J. B. M. COPPOCK. M. A. COOKSON.

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Purpura Complicating Pregnancy

SIR,—I read with interest the article by Dr. J. A. Chalmers (Dec. 11, 1948, p. 1020) on purpura haemorrhagica as a complication of pregnancy but cannot agree with some of his conclusions. In a review[1] of the available literature on this subject in 1943, descriptions were traced of 68 cases of purpura during pregnancy, 75 cases having been stated to have been reported up to that time. It was shown that of the described cases only 5 could be classified as true thrombocytopenic purpura—the rest being purpuric manifestations of a variety of septic and toxic conditions. Some, indeed, were shown to be clinically cases of scurvy.

In the 5 true cases (which included one C. W. F. Burnett and I reported) all the mothers recovered completely. Hence true purpura complicating pregnancy does not appear to be a fatal condition. The fatalities occurred among the other cases, where the purpura was associated with such conditions as septicaemia and poisoning by various drugs. Furthermore, in the 5 true cases treatment varied in each case (in one case splenectomy was performed), but there were no fatalities, and spontaneous and complete recovery followed parturition in all cases. Treatment apparently has little influence upon the ultimate outcome. The amount of post-partum haemorrhage was in no case excessive, and it is obvious that efficient uterine contraction is still the factor of paramount importance in the prevention of haemorrhage.

In the case reported by Burnett and me the initial symptoms of severe epistaxis and widespread ecchymoses appeared at the

fourteenth week of pregnancy, and a platelet count at that time showed 15,000 platelets per c.mm., and at no time during the remainder of the pregnancy did the count rise above 163,000 per c.mm. At delivery the count was 76,000 per c.mm., and yet despite a perineal laceration there was no undue loss and the puerperium was uneventful. The infant's platelet count at the end of the first week was 332,000 per c.mm., and the mother's count gradually returned to normal over the ensuing 6 months. At no time did the patient have any specific treatment for her purpuric condition.

It appears, therefore, that (1) the figures quoted by Dr. Chalmers are not all cases of true purpura, and (2) there is nothing in the available literature to support the statement that the mortality rate is high or to provide any basis for dogmatic principles of treatment.—I am, etc.,

Manchester. I. KLASS.

REFERENCE

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Retaining Patency of Veins

SIR,—The method described by Drs. A. J. Palmer and A. H. C. Walker (Dec. 4, 1948, p. 985) for ensuring patency of veins after cutting-down for transfusion, while no doubt effective, is too complicated to become generally adopted. It also suffers from the disadvantage that the wound is not closed while the cannula is *in situ*, hence presumably the reference to infection of the wound. The sutures described are designed to prevent leakage from the vein after removal of the cannula, but the same end can be achieved by direct pressure of a dressing.

A simple method of ensuring patency of veins after cutting-down is as follows: The vein is exposed in the usual way and the distal part tied off with silkworm gut or with some other non-absorbable suture material, the ends of which are left long. The cannula is inserted and tied in the vein the same way. The wound is then almost closed with one or two skin sutures, and the long ends of the ties on the vein are brought out of the wound alongside the cannula. In order to take out the cannula, the suture fixing it is pulled on until the knot appears and it is then cut out with fine scissors. The suture tying off the distal end of the vein is removed in the same way, and immediately a pressure dressing is applied. Surprisingly little bleeding occurs, and the wound in the vein seals off rapidly. Advantages claimed for this method are simplicity, closure of wound at time of insertion of cannula, and the avoidance of buried catgut.

I would emphasize that in routine ward work cutting-down should be the last resort, and where possible a needle or trocar and cannula should be used. These latter methods often fall into disrepute because of inadequate immobilization of the arm, causing displacement of the needle. This state of affairs is largely due to the fact that it is commonly believed it is possible to immobilize a limb with one back splint. Experience, however, shows that to ensure immobility of the limb at least three splints in the form of a box are necessary, or, alternatively, a light plaster cast should be used.—I am, etc.,

Halifax. A. W. FOWLER.

Calcified Cyst of Spleen

SIR,—Mr. J. H. Donovan's article (Dec. 25, 1948, p. 1106) records an interesting case of calcified cyst of spleen. He points out that his is the second case recorded in this country. This prompts me to mention that Mr. J. I. P. James and I published a case of calcified non-parasitic cyst of the spleen in 1943.[1] Cysts of the spleen present diagnostic difficulties, and in our case diagnosis was made before operation mainly on radiological evidence. The radiological features were: a round cyst in the left upper quadrant the size of a large orange, with a calcified rim, elevating the left diaphragm; the barium-filled stomach was pressed upon by the cyst and pushed to the right; the splenic flexure was displaced downwards. Intravenous pyelogram showed downward displacement of the left kidney. These radiological signs seem to be characteristic of splenic cysts, since they have also been described by other authors. Benton[2] suggests that the downward displacement of the splenic flexure is almost pathognomonic of large cyst of the spleen.

Calcified non-parasitic cysts of spleen are usually believed to be the result of trauma. Although no history of injury could be obtained in our case, signs of old haemorrhage were found in the calcified cyst. In Dr. R. W. Bazeley's case,[3] referred to by Mr. Donovan, a severe accident with fracture of the left lower ribs preceded the detection of multiple calcifications and of a large calcified cyst of spleen. On the evidence of the severe injury to the left lower chest and the presence of a large calcified cyst in the left upper quadrant with pressure signs on neighbouring organs similar to those seen on the radiographs in our case, I felt justified during the discussion on the case in suggesting a diagnosis of calcified cyst of spleen of traumatic origin.—I am, etc.,

London, W.1. A. ELKELES.

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Dracontiasis

SIR,—I read with great interest Dr. W. L. M. Perry's report from Nigeria (Dec. 25, 1948, p. 1107) of his operation on a left inguinal hernia associated with a female specimen of *Dracunculus medinensis* in the hernial sac. In view of the comment that no previous record was available of the occurrence of guinea worm in this situation Dr. Perry and others amongst your readers in the Tropics might be interested in a similar case report which I submitted from Hyderabad (Deccan) and which was published in these columns (Sept. 16, 1933, p. 528).

The points of clinical interest in my own case (which was, I felt, quite inadequately presented through a very scanty knowledge of helminthology and a complete lack of access to the literature of the subject in such localities) were these: an indirect right inguinal hernia containing small intestine and gangrenous omentum was strangulated with the guinea worm, a female 52 cm. long and alive, in close relation to the neck of the sac; a hydrocele present on the same side was also dealt with. A welcome feature of the operation was the unaccustomed ease with which this long worm came out intact, without any need for having recourse to the usual dodges, such as injection of mercuric chloride solution, for facilitating its extraction. The patient's convalescence was uneventful.—I am, etc.,

Huddersfield. W. E. THOMPSON.

Steroid Metabolism and Frontal Lobes

SIR,—Dr. F. Reitman (Dec. 18, 1948, p. 1064) publishes a series of twelve 17-ketosteroid urinary estimations (based on the biochemical work from Charing Cross Hospital[1]) both before and three to four months after bilateral prefrontal leucotomy. It is interesting and instructive that the 17-ketosteroid results from this operation should conform on the whole to those obtained from unilateral adrenalectomy. In his series the average drop was from 13.4 mg. a day to 9.47 mg. a day, and Cases 9 and 10, with ketosteroids of 23.6 mg. and 20.3 mg. a day, look suspicious of cortical overactivity. In our last published analysis[2] of unilateral adrenalectomy the drop in the excretion of 17-ketosteroids in the cases in Group II (post-pubertal virilism) was as follows:

	Pre-operative	Post-operative
Average of 41 tests	17·6	8·5
Good results	17·5	6·8
Improved	19·1	9·9
Remained the same	15·1	8·4

As a general observation we regard a drop of 50% or over associated with the better results. The clinical results in this series were:

	Group II	Cushing's Type	Psychological Symptoms Present
Cases	88	14	15
Good	16	2	3
Improved	45	11	8
Remained the same ..	10	1	2
Deficient information ..	14	—	—
Died from other causes ..	3	—	—

Dr. Reitman does not go into any clinical details, but we have experienced psychosomatico-sexual changes of varying degree in a fair number of patients, and most of them have benefited by unilateral adrenalectomy.

An extreme case of this kind was described in 1939,[2] and the patient has remained perfectly well and was last seen a year or two ago. There is this curious twin control in the evolution of sex precocity and Cushing's syndrome, where the syndromes may respectively emanate from a hypothalamic tumour or basophil adenoma of the pituitary, or both from hyperplasia or tumour of the adrenal cortex, associated with increased output of androgens, which establishes the differential diagnosis. Now it would seem that the pituito-hypothalamic mechanism may be controlled by frontal impulses as far as the excretion of androgens is concerned, vicariously or direct from their production in the adrenal cortex.—I am, etc.,

London, W.1. L. R. BROSTER.

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Toxicity of Soluble Phenytoin

SIR,—As I was going through the article by Dr. T. N. Nauth-Misir (Oct. 2, p. 646) I was reminded of a similar case under my care.

A patient, 32 years old, had been an epileptic for the last 16 years and had potassium bromide, phemitone, phenobarbitone, and phenytoin sodium in various doses at different times. In spite of that he used to get attacks quite frequently. He came under my observation from December, 1946. I started with 1½ gr. (0.1 g.) of phenobarbitone daily in three divided doses. Still his fits were not controlled, so I advised him to have one capsule (0.1 g.) of phenytoin sodium and 1 gr. (65 mg.) of phenobarbitone. He had such a line of treatment for two and a half months. In spite of this he used to get fits once a month or so. I increased the dose of phenytoin sodium to two capsules a day, with 1 gr. of phenobarbitone. Even after this there was no change in the frequency of attacks. He came to see me on Oct. 7, 1947, complaining about his unsteady gait and headache. On questioning he told me that this had started on Oct. 3, 1947, and now he was completely incapacitated. On examination I found that he had cerebellar ataxia, but I could not come to any conclusion about the causation of the condition. I examined him again and noticed that he had hypertrophy of gums. It was now quite clear: he had been having phenytoin sodium two capsules (0.2 g.) daily for seven months. The drug was stopped and he completely recovered in four days. No other measures were taken.

My case differs from Dr. Nauth-Misir's case in that my patient had cerebellar ataxia after such small doses as 0.1 g. daily for 2½ months and 0.2 g. daily for seven months, while his was a case of an acute severe toxic reaction (with cerebellar ataxia, etc.) after a single heavy dose of 250 tablets of 0.1 g.—I am, etc.,

Ahmedabad, India. S. C. KUSUMGAR.

Temperature Recording

SIR,—I have read the interesting article on temperature recording in children by Professor Alan Moncrieff and Dr. B. J. Hussey (Dec. 4, 1948, p. 972) and the comments in the annotation (p. 991) on this particular subject. It seems that despite the fact that temperature recordings have been common routine for centuries there are still differences of opinion on the various ways to record temperature and their significance.

In this connexion I would like to mention that temperature differences exist not only at various sites but even under the axilla if taken at the same time on both sides. I have been taking bilateral axillary temperatures in cases of pulmonary tuberculosis for some time and recorded differences. The differences seem to be connected with underlying disease in the chest, and they vary from fractions of a degree to 1° C. In cases of unilateral disease the temperature is higher on the side affected, and in bilateral disease on the side of greater activity. The differences are more manifest if recordings are made over a period of ten days—taking temperatures morning and evening on both sides for ten minutes with ordinary mercury thermometers.

Before inducing an artificial pneumothorax in cases of bilateral disease, besides other factors I find it useful to take bilateral temperatures, and I start an artificial pneumothorax on the side where greater activity is indicated by the average higher temperature.—I am, etc.,

Harold Court Sanatorium, Essex. M. WEINBERGER.

POINTS FROM LETTERS

Diagnosis of Tuberculous Meningitis

Dr. P. E. FITZPATRICK (Belfast) writes: I was extremely interested in Dr. J. T. Lewis's letter (Dec. 11, 1948, p. 1036) on the early diagnosis of tuberculous meningitis by cerebrospinal fluid examination, especially in relation to the fall in the glucose content. What to my mind is equally important is the recognition of early clinical signs and symptoms, as this leads to earlier hospitalization and therefore earlier examination of the C.S.F. and earlier treatment. I have in mind four cases of this disease which had, all of them, the same signs and symptoms. All four were boys of age group 5–10 years. In all a family history of pulmonary tuberculosis was present. In each case, about three months before the onset of the cerebral symptoms of headache, vomiting, photophobia, strabismus, etc., it was noticed that there developed on the hands, trunk, and knees particularly a crop of small papillomata, not unlike molluscum contagiosum, irregularly distributed. Associated with this were irritability and lassitude, with a disinclination to play games or to take an interest in toys. Inside three months all developed variable symptoms—mostly headache, intermittent temperature, occasional vomiting, and what to my mind was most significant of all, night terrors. Having the possibility of tuberculous meningitis in mind, I sent all four to hospital with a tentative diagnosis of tuberculous meningitis. In each case this was confirmed by the presence of tubercle bacilli in the C.S.F. and a reduced glucose content. It would be interesting to know if this crop of small papillomata might be the skin manifestation of the mass dissemination of some abdominal, pulmonary, or other focus of tubercle bacilli, affecting at the same time the meninges and later producing all the signs and symptoms of tuberculous meningitis.

Herpes Zoster

Dr. EDGAR PALMER (Lydd, Kent) writes: The treatment of this distressing complaint has been characterized by many different procedures and has been unsatisfactory in the past. As it is known that it is due to inflammation of the posterior nerve roots caused by a virus, and as it is also known that hexamine is excreted into the nerve sheaths, it seemed reasonable to prescribe this drug. Over a period of ten years in a rural practice, without the controls possible in a hospital I have found that tab. hexamine gr. 5 (0.32 g.) t.d.s., p.c., has given most excellent results, causing the lesions to dry up quickly and the irritation and pain to subside rapidly. I have not had a case of post-herpetic neuralgia since using this drug.

Temperature Recording

Dr. S. L. FRANK (Preston) writes: From recent correspondence there seems to be some doubt as to how long a thermometer should be left in position. This must vary from case to case, as the rate of heat transference from the tissues to the thermometer bulb is variable and depends on such variable factors as the degree of dilatation of the blood vessels concerned. Thus in a suspected appendicitis, where the expected pyrexia is only slight and the peripheral vessels may be constricted from some degree of shock, it may be well over five minutes before equilibrium is reached between the oral temperature and the temperature of the mercury. It follows that the only correct way to take a temperature (irrespective of the site used) is to wait until the mercury stops rising—in practice, until two successive half-minute readings are the same. In teaching this method I have found it necessary to ensure that the thermometer is not shaken down between each half-minute reading.

Clouding of Surgeons' Spectacles

Dr. C. G. KAY SHARP (Leeds) writes: With reference to the letters on this subject from Mr. G. K. Rose (Dec. 4, 1948, p. 998) and Mr. R. Wood Power (Dec. 25, 1948, p. 1123), may I draw attention to the fact that the problem of clouding of spectacles has been solved by the provision of contact lenses? The lenses are kept free from clouding by the movement of the eyelids. The average continuous wearing time is four hours—long enough for most surgical sessions.

Procaine Penicillin

Dr. L. GREENFIELD (London, N.5) writes: The introduction of procaine penicillin suspension has solved many of the difficulties of penicillin administration in general practice. The handling of the suspension, however, presents a difficulty which to some extent neutralizes the advantages. At present the substance is exhibited in rubber-capped bottles from which aspiration into the syringe even through a wide-bore needle is not easy. There seems to be no reason why it should not be presented in 1 ml. ampoules, from which the suspension could be aspirated into the syringe with the needle detached. The injection into the patient, using a needle of as small a bore as size 12, offers no difficulty and causes little discomfort.

Obituary

R. H. MILLER, M.D., F.R.C.P.

Dr. Reginald Henry Miller, who died in hospital in London on Dec. 23 at the age of 69, was consulting physician to St. Mary's Hospital, London, and the Paddington Green Children's Hospital.

The son of Dr. Andrew Miller, of Hampstead, he was educated at Charterhouse and at St. Mary's Hospital. He graduated M.B. in 1905 and proceeded M.D. in 1907. Dr. Miller was a general physician with a particular interest in paediatrics. He was medical registrar and pathologist at the Hospital for Sick Children, Great Ormond Street, in 1906–8, and he acted as secretary of the Section of Diseases of Children at the annual meeting of the B.M.A. in 1911. He was elected F.R.C.P. in 1917, and was an original member of the British Paediatric Association and an honorary member at the time of his death. He was the first editor, together with the late Dr. Hugh Thursfield, of the *Archives of Disease in Childhood*, and himself contributed a number of important articles to the literature on diseases of children.

Dr. Miller was a recognized expert on mental deficiency in children and a visitor for the County of Middlesex under the Mental Deficiency Acts. He also wrote extensively about rheumatic fever and heart disease in childhood. At Paddington Green he was responsible for starting the first supervisory clinic for rheumatic children in the London area. In 1939, soon after the outbreak of the recent war, he left London to become medical director of the Park Prewett General Hospital at Basingstoke.

Dr. T. Pearse Williams writes: The passing of Reginald Miller removes one more of that group of physicians who by their writings, based largely on clinical observation, did much to advance the art of paediatrics in the first thirty years of this century. I first met Reginald Miller in 1919 at St. Mary's, and later became a colleague of his at Paddington Green Children's Hospital. His fine figure, commanding presence, and resonant voice were combined with a ready wit and extensive knowledge of our language. His carefully chosen comments at committees were at times devastating, and he coined some most pertinent aphorisms. It was at Paddington Green that Miller carried out most of his work on the coeliac disorder, gastromegaly, and juvenile rheumatism. He discussed his problems freely with his colleagues, particularly with H. W. Perkins in the pathological department. Miller had a childish love of car riding, and for some years I called for him regularly to drive him to his rooms in Harley Street where, except for his hospital visits, he spent most of his days. I also lunched with him regularly and gained much from the breadth of his knowledge, his ready sympathy, and his interest in the development of paediatrics, particularly with the foundation of the British Paediatric Association. Miller's disposition was shy and sensitive, often masked by remarks apparently rude but rarely intended to be so. In 1911 he published a textbook, *The Medical Diseases of Children*, a copy of which I have before me. I doubt if any more recent publication has surpassed it in quality. He was much hurt by criticism which he felt was unfair and unjust, and could never be persuaded to revise the text for a further edition. A sincere Catholic, he yet had much of the Puritan in his nature and was almost ascetic in his habits. He worked quietly and unhurriedly, typing all his own letters, for neatness was a passion with him. His relaxation in the summer was a visit to Lords. He talked much of his family, in whose development he gained much happiness. His transfer to Basingstoke in 1939 broke the steady routine of his life, and he was little seen in London thereafter. Despite much importuning of his colleagues at Paddington Green, he never returned to take up work there, much to our regret. For much personal kindness I could never adequately repay him, and at the Children's Hospital we mourn the loss of a very dear friend and colleague.

Dr. Thomas Hunt writes: As a physician Reggie Miller possessed the great gift of recognizing serious illness almost instinctively, and, though there might be little to suggest it to others, he seemed at once to be able to pick out the important from the trivial. He was essentially humble in his own estimation, and was never impatient in listening to the views of others, however junior. His patients were devoted to him, and his gentle kindness on his ward rounds was an inspiration to students. As a teacher he will be long remembered for his wit and paradox and his quickness at finding the *mot juste*. At times his lazy, almost flippant, manner and his large build —he was over 6 ft. 3 in.—seemed to give an impression of indifference; indeed, with minor ailments he could be frankly bored. But with an ill patient or an anxious relative he showed that understanding and sympathy which was part of his own gentle nature. As a man he hated violence and bustle, and both wars were a great ordeal to him. By temperament he was sensitive and cautious, with many of the attributes of the artist. His health was not good, and for some years before his death he had had to take care of himself and avoid strain and over-exertion. Miller was at his best with children, and his work on coeliac disease, duodenal ileus, and especially rheumatic fever was outstanding. He had little sympathy with much modern psychiatric teaching, and in particular disapproved of the Freudian school, but his views on the psychosomatic aspects of disease were in many ways remarkably ahead of his time. Miller was an expert prescriber, with a remarkable memory for mixtures and doses, and he used medicines with skill and a fine regard for their value as well as their dangers. Reggie Miller was one who, though he could be biting and even sarcastic if it was necessary, nevertheless delighted in saying nice things about others; in return he was almost childishly happy at knowing of his friends' affection and at feeling that he was welcomed and appreciated. His many friends will mourn the loss of a personality whose charm, wit, brilliant conversation, and gentle nature will not soon be found again.

WILLIAM SUSMAN, M.D.

Dr. William Susman, who died suddenly on Dec. 23 at the early age of 53, had been for many years lecturer in morbid anatomy and histology in the University of Manchester. He was a graduate in arts and medicine of Queen's University, Kingston, Ontario, and his interest in pathology was already obvious in his student days. After qualifying in 1923 he was awarded a Hoffmann fellowship and spent two years in Edinburgh, where he studied under Lorrain Smith and held a number of junior appointments in the pathological departments of the University, the Royal Infirmary, and the Royal Mental Hospital. In 1925 he went to Manchester as assistant lecturer in bacteriology in the department of pathology under Shaw Dunn. In recent years his main hospital appointments had been those of senior pathologist to the Manchester Royal Infirmary and honorary pathologist to the Manchester Royal Eye Hospital.

Dr. Susman was a keen research worker and published some twenty-five papers. Many of these reflect his special interest in diseases of the ductless glands and include a classical paper on atrophy of the adrenals as a cause of Addison's disease which was published in the *Journal of Pathology and Bacteriology* in 1932. His paper on intraocular tumours, which appeared six years later in the *British Journal of Ophthalmology*, has also been recognized as outstanding. In recent years administrative work, both within and outside the University, had claimed much of his time. He was an active member of the Board of the Faculty of Medicine and of its various committees. A member of the British Medical Association since 1924, he was a member of the Non-Professorial Group Committee from 1937 to 1946, of the Special Practice Committee in 1938–9, and of the Special Committee on Patents in 1944–5. Medical lecturers throughout the country have reason to remember him gratefully, for he was largely instrumental in founding the Association's Non-Professorial Group, which grew steadily in strength and influence under his chairmanship.

A vigorous and effective teacher of morbid anatomy and histology, Dr. Susman had a clear grasp of the needs of the medical student, and he never lost the zest and freshness that keep teacher and student in contact. Many generations of students will remember him with respect and affection. His great experience was always freely at the service of his colleagues and others, and his loss as a consultant will be widely felt.

From 1915 to 1919 Dr. Susman saw service in the Canadian Army Medical Corps, in the 8th and 2nd Duke of Wellington's

Regiment, and in the Royal Flying Corps, and he was twice wounded; in the recent war he served as a medical officer in the Home Guard. He is survived by his wife and one son, a student of medicine, and to them all who knew him will desire to express their sympathy.

Dr. JOHN MOFFAT LOGIE, of Burntisland, died on Dec. 20, and with his passing Fife has lost an outstanding personality in the medical profession. He was proud of the fact that he came of humble stock, and, in his own words "*per vias duras*," he qualified as a chemist and with his savings went on to graduate M.B., Ch.B. at Edinburgh University in 1910. For a time he was a house-surgeon at the Royal Infirmary, Dundee, and then he settled first in Aberdour, later moving to the neighbouring busier town of Burntisland. From there Dr. Logie conducted a large general practice and endeared himself to many patients. He was medical officer of health to the town of Burntisland—one of the few remaining medical officers of smaller burghs. He was the embodiment of all the good qualities which go to make a first-class family doctor. So successful was his medical career in his own town that he received a public presentation on his recent retirement. Dr. Logie read widely, and was a keen student of the classics all his life. He was an active member of the B.M.A. in Fife, and took a great interest in its work. His contributions to discussions were always marked by his complete honesty of purpose and opinion. He was a past president of the Fife Branch. A sincere churchman, he was closely identified with the affairs of St. Serf's, Burntisland, where a memorial service for him was held on Dec. 22 and attended by many of the local people. He is survived by his wife and daughter, to whom we offer our sympathy.—J. M.

Dr. ARTHUR ANDERSON, who was senior medical officer of the Glasgow Education Health Service, died on Dec. 22 at his home in Victoria Park Gardens at the early age of 53. Dr. Anderson was an M.A. of Glasgow University and graduated M.B., Ch.B. in 1922. He proceeded M.D. in 1924, and took the D.P.H. in 1943. He was appointed senior medical officer only in January, 1948, but more than twenty-four years of his professional career had been devoted to the Glasgow Education Health Service. During this time Dr. Anderson made a special study of rheumatic disease in school-children, and he was expert in eye conditions and refraction. One of his greatest interests was in the nutrition of the children, and he was ever watchful that the school meals should provide a good-balanced diet. At the time when he acted as school medical officer for the Partick area he knew practically every child and parent in his district. Dr. Anderson was held in the highest esteem by his colleagues and was popular with teaching staff and pupils alike. On the appointment of the late Dr. J. Miller Young as senior medical officer of the Education Health Service, Dr. Anderson was appointed senior assistant medical officer. He was a good administrator and assisted materially in the building up of the department to meet the provisions of the recent Education Act. He was an elder of Partick Parish Church and an active member of the Partick Medical Association. He had few hobbies outside his work, to which he gave his whole attention. During the war years Dr. Anderson trained many hundreds of the citizens of Glasgow in the essentials of A.R.P. and first-aid. He is survived by his wife and a daughter.

Dr. GEORGE HENRY CHAVASSE MOLD died on Dec. 24 at the age of 64. Dr. Mold studied medicine at Birmingham University, and graduated M.B., Ch.B. in 1908. After a brief period as a house-physician at the General Hospital, Birmingham, he went into general practice. During the 1914–18 war he served as a captain in the R.A.M.C., and not long after demobilization he settled in Sussex.

G. S. writes: Dr. Mold came to Cross-in-Hand, Sussex, over nineteen years ago, and a few years later we became partners. One could not have had a more loyal partner, nor a more conscientious or harder worker. He never spared himself in spite of ill-health during his last few years here. He served on the National Insurance Committee for East Sussex and helped in Red Cross work. He found a home to retire to in Gloucestershire, where he was enjoying his garden and a well-earned rest. His last illness came unexpectedly, and although he knew the end could not be long delayed he bore it very bravely and showed great courage. Even a week before he died he dictated part of a letter showing interest in old friends here.

Dr. KASARGOD SOMANATH BHAT died recently at Karkala, South Kanara, Madras Province, India, at the age of 63. Dr. Bhat, who studied medicine at Madras and later at St. Bartholomew's Hospital, qualified in 1915, and was in practice in S.E. London for many years. During the war he acted as medical officer for a number of the Bermondsey shelters. He returned to his native province only in 1944.

Dr. K. Malik writes: Dr. Bhat was my friend during the last twenty-six years. He did for me and a number of others in the same circumstances a great service—namely, gave me a start. He not only bought instruments, including a dental chair, but sent us patients. He was always gruff, monosyllabic, and not too well dressed, but he worked hard and gave generously. His learning was very wide. He always knew the latest medical literature, the best articles on chess, and he was interested in botany. His type is rare. He never spoke of his good deeds, but I discovered many, always in roundabout ways—although I saw him for many years at least once a week. The world is the poorer for his loss and many of us are the sadder.

Dr. Cranston Walker writes: To students Arthur Robinson (Dec. 18, 1948, p. 1084) had many outstanding characteristics. The movements of his spare figure were quick, energetic, and accurate. His decisions also were quick, and his intentions proceeded immediately and smoothly into action. He never seemed to waste a moment. His speech, though quiet, was equally quick and efficient. His manner of entering the dissecting-room was an economical rebuke, considerably effective, to anyone who lounged or slouched. He disallowed smoking there. His knowledge of human anatomy was amazing, and his understanding profound. He knew the body with intimate familiarity, not only as it is usually placed and described, but in any attitude, and from any aspect or direction, in broad view or in the minutest detail. He could answer any question, however recondite, without an instant's hesitation, and apparently with complete infallibility. Evidently he had prepared himself for his work of teaching anatomy with most exacting thoroughness and devotion. He probably had great powers of visualization, and in three dimensions; so that in his mind any structure under attention stood out solid in a translucent body, and round it he could see vividly, as he liked, any other structures, and could remove them, replace them, or render them transparent at will in order to make plain any matter of structure or relation. His blackboard drawings were done with great rapidity. He appeared to be building up structures, or occasionally cutting down on them, according to the solid images in his mind, not drawing after memorized diagrams. He often used the broad surface of the chalk to cover areas quickly, subordinating the use of outline. He carried on research with persistent vigour, especially in embryology, but never allowed this to encroach on his teaching. His devotion to this, and to the needs of anatomy students at all stages, was so eager and so successful that infection with his zeal was inescapable. It was perhaps most felt in his informal dissecting-room tutorials. He had no need to assert authority; his manner was always that of a helpful energetic friend—who had given considerable attention to anatomy—leading suavely to knowledge and understanding.

Medico-Legal

VISCERAL TRANSPOSITION AS A DEFENCE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

A young man on trial for murder in the Central Criminal Court in Dublin recently adduced a defence that had probably never been attempted before: that he was a case of transposition of the viscera and therefore incapable of a normal degree of self-control.[1] He was 28, and for about eighteen months had been keeping company with a widow of 35, to whom he was passionately attached. He was drawing a small wage as a chemist's assistant, and had just failed to pass an examination which would have advanced him professionally. In a field which the couple used to frequent they had—according to the accused—a quarrel, but of an unimportant kind. The woman spoke of leaving him; there was some sort of a struggle in which they both lost their footing, and he found his hands round her throat and, without being able to control what he was doing, continued to squeeze it until she lost consciousness. He then felt the heart, dragged the body some distance by the hands, and repeatedly kicked the face, breaking the bones. He made no serious attempt to divert suspicion from himself. He maintained that he had never intended to do her any harm and that something had snapped in his brain.

A general practitioner of Ballybunion, Dr. John Hannan, gave evidence that he had known the accused from his youth,

[1] *Dublin Evening Herald*, Oct. 18-22.

and that the mother had consulted him because her son had been backward and solitary. He said that the lad's physical development had been poor and he had complete transposition of the viscera. Dr. Hannan maintained that this rare condition was often associated with mental deficiency, and put forward the theory that it was a sign of a throwback to a more primitive type of ancestor, and that a person affected by it could therefore not be expected to have the same restraint over his emotions as an ordinary person. He declared his belief that the accused at the moment of the murder had been temporarily insane and reverted to a jungle type. The prison medical officer, Dr. T. Murphy, confirmed the transposition but said that this abnormality, though rare, had no significance and was found in perfectly healthy people.

The judge directed the jury that there had been no evidence of provocation, and so the defence of manslaughter, on which the accused also relied, would not stand. Moreover, no reasonable jury could in his opinion accept any of the evidence tending to show insanity. Some people did insane things from time to time under the stress of emotions or passion, but their lack of self-control did not absolve them from responsibility in law for their acts. To prove insanity an accused person must show that because of a defect of reason he did not know what he was doing, or did not know that it was wrong (the M'Naghten rules); otherwise he was responsible. The jury, after an absence of an hour and forty minutes, came back with a verdict of guilty and a strong recommendation to mercy. The sentence of death has since been commuted to penal servitude for life.

Universities and Colleges

UNIVERSITY OF LONDON

H. F. T. Deane has been approved at the examination for the Academic Postgraduate Diploma in Medical Radiology.

UNIVERSITY OF MANCHESTER

William Francis Nicholson, M.D., M.Chir., F.R.C.S., has been appointed Lecturer in Surgery in the University.

UNIVERSITY OF LEEDS

The Council of the University has appointed Thomas Duncan Day, M.D., as Senior Research Fellow in Experimental Pathology and Cancer Research.

UNIVERSITY OF BRISTOL

D. M. P. R. Clarke has been approved in Part II of the examination for the Diploma in Medical Radiodiagnosis.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on Dec. 15, with Mr. Frank E Jardine, President, in the chair, the following, having passed the requisite examinations, were admitted Fellows:

T. M. Abbas, S. Abel, A. F. Alexander, P. St. G. Anderson, R. W. Bailie, J. A. Barclay, A. E. Bateman, H. A. Benjamin, C. L. Beynon, S. C. Bhattacharyya, H. G. Biggart, H. D. W. Black, J. S. Boyd, I. Bruce, A. Buchan, G. Buchanan, J. S. Calnan, J. D. Cameron, J. A. Campbell, N. A. Campbell, J. S. Cason, Z. A. Choudhuri, K. S. Clarke, K. W. Cochrane, R. B. G. Cook, J. W. Cowie, C. S. Dafoe, K. H. Dalrymple, W. J. Dempster, W. R. Dickie, C. A. P. Donaldson, A. G. Gibb, C. A. Gleadhill, A. G. Gray, L. M. Green, W. S. Hanna, P. Harris, A. R. Harper, C. J. Hassett, J. R. Hochhauser, V. S. Hughes-Davies, R. F. Jackson, E. W. Jeyaratnam, A. Joffe, A. M. Keith, J. R. Kenyon, D. R. Kilgour, S. S. Kirtane, A. P. Kitchin, J. W. Knox, T. Koonvisal, D. W. Lamb, A. S. Lewis, R. A. Lindsay, Ursula M. Lister, H. K. Lucas, J. T. Mair, R. N. G. Majumder, T. S. Matheson, A. J. M. Mathieson, A. B. May, R. K. Menda, I. H. Meyer, A. M. Michael, J. P. Mitchell, R. Morrison, J. Mowat, A. A. Murray, J. H. McBeath, R. J. M. McCormack, A. B. McCulloch, D. M. Macdonald, G. H. D. McNaught, C. G. Nairn, J. G. Napier, E. L. Nicolson, T. H. Norton, W. D. Paterson, B. H. Price, Ghias-Ud-Din Qazi, P. T. Quinlan, M. S. Qureshi, Florence C. R. Richardson, E. F. Ridley, L. R. Robson, P. E. Roland, N. Rosenzweig, A. M. Sadek, H. K. Sarkar, A. S. Scott, L. S. Scott, R. H. Sewell, Shrikrishna, J. J. Skapinker, A. D. Smit, P. H. E. Smith, E. F. G. Stewart, B. A. Thompson, G. R. Thomson, N. Tunnell, P. R. Walbaum, R. B. Watson, Catrin M. Williams, R. G. Williams, Eileen D. M. Wilson, D. Wright, J. H. Wrigley, S. Zinn.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

Dr. H. C. Cameron, F.R.C.P., will deliver the Dr. John Burns Lecture in the Hall of the Faculty (242, St. Vincent Street, Glasgow) on Wednesday, Jan. 12, at 5 p.m. The title of the lecture is "The Beginnings of Modern Surgery, with personal recollections of Lord Lister." All medical practitioners are invited to attend.

Medical News

Inquiry into Punishment

The Home Secretary has appointed a committee to review the existing methods of punishment in prisons, Borstal institutions, approved schools, and reform homes (other than corporal punishment in prisons and Borstal institutions); to consider the procedure adopted in inquiries into breaches of discipline; and to recommend whether changes in methods and procedure are necessary or desirable. The members are Mr. H. W. F. Franklin (chairman), head master of Epsom College; Mrs. D. M. Bates, chairman of Leicester City Probation Committee; Dr. R. D. Curran; Mr. J. C. Jolly, K.C., Recorder of Preston and member of the Home Office advisory council on the treatment of offenders; Sir Leo Page, member of the Home Office advisory committees on probation and treatment of offenders; and Mr. E. V. Watering, member of the National Union of General and Municipal Workers. The joint secretaries are Mr. D. Pettigrew, of the Prison Commission, Horseferry House, Thorney Street, London, S.W.1, and Mrs. M. G. Kewley, of the Children's Department, Home Office, S.W.1. Anyone interested in the work of the committee is invited to communicate with one of the secretaries.

Dr. Curran, who is an authority on the medical aspects of crime, holds the post of psychiatrist at St. George's Hospital. He qualified in 1927, taking the Cambridge degree and the M.R.C.P. a year later, and the D.P.M. in 1930. He was elected F.R.C.P. in 1937. He served throughout the recent war in the R.N.V.R. as Consultant in Psychiatry.

Lock on Dangerous Drugs

New regulations made by the Home Office make it the duty of doctors, chemists, and other authorized persons to take proper care of dangerous drugs. The Home Office states that the courts will determine in any individual case what degree of professional necessity would justify an authorized person in carrying or leaving unattended any dangerous drug which is not in a locked receptacle, but there would seem to be no need for the prosecution to prove negligence when drugs are found otherwise than in a suitable receptacle. The Home Secretary is advised that a car cannot be regarded as a receptacle.

Administration of Water Undertakings

The Ministry of Health has issued a new version of its "Memorandum on the Safeguards to be Adopted in Day-to-Day Administration of Water Undertakings" (H.M.S.O. 2d.). It has been revised in the light of recommendations of the Gathering Grounds Subcommittee of the Central Advisory Water Committee. Where the water supply comes from the headwaters of the stream or an intake near the source, the water undertakers should if possible obtain control of the gathering ground above the dam or intake and so manage the land as to prevent pollution. When control of the gathering ground cannot be obtained, the water undertakers should frequently inspect it and seek the co-operation of farmers and householders there, as well as of the local authority, to ensure that sewage and manure are properly disposed of.

Wills

Dr. Charles Morley Wenyon, late Director-in-Chief of the Wellcome Research Institution, left £6,593. Dr. Francis Benjamin Sutherland, formerly deputy commissioner of the General Board of Control for Scotland, left £8,358. Miss Eugenie Leeson Willis, F.R.C.S., who was chief assistant to the orthopaedic department at the Manchester Royal Infirmary, left £2,656.

COMING EVENTS

Society of Medical Officers of Health

The second annual dinner of the Services Hygiene Group of the Society of Medical Officers of Health will be held at the Quadrant Restaurant, 74, Regent Street, London, W., on Friday, Jan. 28, at 7 for 7.30 p.m., with the president, Colonel H. D. Chalke, in the chair. All past and present hygiene officers of the Services are cordially invited, whether members of the society or not. Applications for tickets (13s. 6d., including gratuities but exclusive of wines) should be sent with remittance to the honorary secretary, Dr. G. M. Frizelle, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, as soon as possible. Dress: dinner jackets, with decorations.

Ophthalmological Congress

The Annual Congress of the Ophthalmological Society will be held at the Royal Society of Medicine, 1, Wimpole Street, London, W.1, on March 31 to April 2, 1949. The subject for discussion will be "Corneal Grafting," which will be opened by Dr. R. Townley

Paton (New York), Professor A. Franceschetti (Geneva), Professor G. P. Sourdille (Nantes), and Mr. J. W. Tudor Thomas (Cardiff). Members who wish to take part in the subsequent discussion are advised to intimate their intention before the opening of the Congress. Members wishing to read papers are asked to send the titles to Mr. Bridgeman as soon as possible. Abstracts of papers should be submitted not later than Jan. 31, 1949. The annual dinner will be held on March 31.

Neurological Congress

The 4th International Neurological Congress will be held in Paris on Sept. 5–10, 1949. Scientific business will comprise discussions on four main topics: (1) the thalamus and its pathology; (2) electro-encephalography and electromyography; (3) virus diseases of the nervous system; (4) the surgery of pain. Short papers on any neurological topic will also be given, and members are invited to submit by Feb. 1, 1949, titles and an abstract of their communication to the secretary (Dr. Macdonald Critchley, the National Hospital, Queen Square, London, W.C.1). The length of the communication must not exceed ten minutes. No member may give more than two communications. Application for membership and all financial contributions must be made through the national committee for each country, which will transmit all applications for membership and all subscriptions to the General Committee in Paris. There are two classes of members: (1) full members—i.e., all medical men or women interested in neurology, and (2) associate members—i.e., non-medical men or women interested in the Congress. Every member of the Section of Neurology of the Royal Society of Medicine is invited to contribute the sum of 10s. towards the general expenses of the Congress (whether attending or not). The subscription for full members is £2 10s. and for associate members £1 5s. All cheques should be made payable to the Treasurer, International Congress, and sent to Dr. M. J. McArdle, 52a, Wimpole Street, London, W.1, before April 1, 1949.

APPOINTMENTS

J. D. W. Pearce, M.D., F.R.C.P.Ed., D.P.M., has been appointed Assistant Physician to Department of Psychiatry, St. Mary's Hospital, London, W.

Dr. Pearce qualified at Edinburgh University in 1927, and after taking the D.P.M. in 1930 proceeded M.D. in 1933. He took the M.R.C.P.Ed. in the same year, and was elected to the Fellowship in 1937. Dr. Pearce has been specially interested in the psychological problems of delinquency and has contributed to the medical press on the subject.

Robert Barer, M.B., B.S., of the Department of Human Anatomy in the University of Oxford, has been appointed Alan Johnston, Lawrence, and Moseley Research Fellow of the Royal Society for two years from Jan. 1, renewable for a further three years.

Dr. Barer took the London M.B., B.S. with honours in 1942 at University College Hospital and has worked on phase-contrast microscopy, publishing a paper on the subject in the *Quarterly Journal of Microscopical Science* in 1947. He served in the R.A.M.C. during the war, and was awarded the Military Cross. He will continue his work at Oxford on the biological and medical applications of new methods of microscopy, with special reference to the Burch reflecting microscope.

CLIVE, F. TEMPLE, M.B., B.S., Acting Honorary Medical Director of the British Legion Village.

SOCIETIES AND LECTURES

Monday

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, London, W.—Jan. 10, 8.30 p.m. "*Treatment of Osteo-arthritis of the Hip and Knee.*" Discussion to be introduced by Messrs. W. G. Waugh and W. A. Law.

WESTMINSTER HOSPITAL SCHOOL OF MEDICINE, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—Jan. 10, 5.30 p.m. "*Cancer of the Pharynx and Oesophagus.*" Clinico-pathological demonstration.

Tuesday

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 47, Queen's Gate Terrace, London, S.W., Jan. 11, 7 for 7.30 p.m. General meeting. "*Radioactive Isotopes in Treatment.*" Discussion to be opened by Drs. D. W. Smithers and W. V. Mayneord.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Jan. 11, 5 p.m. "*Histopathology of the Skin,*" By Dr. I. Muende.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Jan. 11, 11 a.m. "*Ano-rectal Gonorrhoea,*" by Dr. A. H. Harkness.

PHYSIOTHERAPISTS ASSOCIATION OF GREAT BRITAIN.—At Charing Cross Hotel, Strand, London, W.C., Jan. 11, 8 p.m. "*Physiotherapy and Its Uses in Postural Deformities,*" by Dr. Edward Moore.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—Jan. 11, 5 p.m. "*The Cardiology of Old Age,*" Goulstonian Lecture by Dr. C. J. Gavey, F.R.C.P.

Wednesday

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Jan. 12, 11 a.m., "*Vulvo-vaginitis,*" by Dr. W. N. Mascall.

LONDON UNIVERSITY, Senate House, W.C.—Jan. 12, 5.30 p.m. "*The Influence of General Health Supervision on the Frequency of Dental Caries in Groups of Norwegian Children.*" Special University Lecture by Professor G. Toverud, Director of the Department of Pedodontia in the Dental School, Oslo.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—Jan. 12, 5 p.m. "*The Beginnings of Modern Surgery, with Personal Recollections of Lord Lister,*" by Dr. H. C. Cameron.

SOCIETY OF CHEMICAL INDUSTRY.—Joint meeting of the Microbiological Panel of the Food Group and the Society for Applied Bacteriology, at Medical Society of London, 11, Chandos Street, W., Jan. 12, 2.15 p.m. "*Mycorrhiza and the Growth of Farm Crops,*" by Dr. M. C. Rayner; "*Micro-organisms in Relation to the Production and Degradation of Soil Organic Matter,*" by Dr. G. K. Frazer; "*Soil Antibiotics,*" by Dr. P. W. Brian. Discussion.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, Wandsworth Common, S.W., Jan. 12, 8.15 p.m. "*Diagnosis and Treatment of Acute Mastoiditis,*" by Dr. W. A. Hervey.

Thursday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Jan. 13, 5 p.m. "*The Influence of Stress in Dermatology,*" by Dr. H. W. Barber.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Jan. 13, 11 a.m. "*Gonococcal Infections of Upper Urinary Tract,*" by Dr. A. H. Harkness.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—At 17, Bloomsbury Square, London, W.C., Jan. 13, 7.30 p.m. "*London and Pharmacy in the Seventeenth Century,*" by Agnes Lothian, Ph.C.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—Jan. 13, 5 p.m. "*The Cardiology of Old Age,*" Goulstonian Lecture by Dr. C. J. Gavey, F.R.C.P.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—At Large Lecture Theatre, Jan. 13, 4.30 p.m. Lecture-demonstration: Neurology.

Friday

LONDON CHEST HOSPITAL, Victoria Park, E.—Jan. 14, 5 p.m. "*The Application of Collapse Therapy in Pulmonary Tuberculosis,*" by Dr. N. Lloyd Rusby.

MAIDA VALE HOSPITAL MEDICAL SCHOOL, Maida Vale, London, W.—Jan. 14, 5 p.m. Case demonstration by Professor S. Nevin.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—Jan. 14, 8 p.m. Address by Mr. I. M. Duthie.

WEST KENT MEDICO-CHIRURGICAL SOCIETY.—At Miller Hospital, Greenwich High Road, London, S.E., Jan. 14, 8.30 p.m. Clinical meeting.

Saturday

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital, Gray's Inn Road, W.C., Jan. 15, 3 p.m. Clinical meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTH

Fisher.—On Dec. 29, 1948, at St. George's Hospital, to Mary (Peppin), wife of Dr. R. E. W. Fisher, a daughter.

MARRIAGE

Habibis—Murray.—On Dec. 29, 1948, at St. Mary and the Angels, Bayswater, W., Homer A. Habibis, M.D., D.C.H., of 1a, Porchester Terrace, London, W., and Stella Mary Murray, M.B., B.S., D.C.H., elder daughter of Mr. and Mrs. J. A. Murray, of Strefford House, Brighton Road, Sutton, Surrey.

DEATHS

Abernethy.—On Dec. 26, 1948, at 54, Queen's Crescent, London, N.W., Victor Alexander Abernethy, L.R.C.P.&S.I. and L.M.

Aldridge.—On Dec. 26, 1948, at Bournemouth, Charles Braxton Mooring Aldridge, M.R.C.S., L.R.C.P., of Charford, 100, Richmond Park Road, Bournemouth, aged 71.

Anderson.—On Dec. 22, 1948, at 37, Victoria Park Gardens South, Glasgow, Arthur Anderson, M.D., D.P.H., aged 53.

Balthasar.—On Dec. 29, 1948, Ewald Mouat Balthasar, M.R.C.S., L.R.C.P., D.P.H., of 492, Lea Bridge Road, Leyton, E.

Dockray.—On Dec. 29, 1948, John Vernon Dockray, O.B.E., M.R.C.S., L.R.C.P., of Stradbroke, near Diss, Norfolk.

Ffoulkes.—On Jan. 2, 1949, at Glan Heulog, Abergele, Denbighshire, Meredydd Ffoulkes, M.R.C.S., L.R.C.P., aged 62.

Garrad.—On Dec. 26, 1948, Francis William Garrad, M.D., of 50, Coldbath Road, Harrogate, aged 78.

Hollway.—On Dec. 26, 1948, at Teignmouth Hospital, Edith Blake Hollway, O.B.E., M.B., B.S., of St. Anthony, Bishopsteignton, Devon.

Hutchinson.—On Dec. 25, 1948, at Worthing, Richard Cecil Hutchinson, M.D., D.P.H.

Mackay.—On Dec. 28, 1948, at Cheltenham, James Murdoch Mackay, M.C., M.B., Ch.B., late West African Medical Service.

Miller.—On Dec. 23, 1948, at St. Mary's Hospital, London, W., Reginald Henry Miller, M.D., F.R.C.P., of 32, Abbey Gardens, London, N.W.

Mold.—On Dec. 24, 1948, at Orchard Leigh, Eastington, Glos, George Henry Chavasse Mold, M.B., Ch.B., late of Cross-in-Hand, Sussex, aged 64.

Mossman.—On Dec. 24, 1948, at Baledmund, Pitlochry, Perthshire, Robert Arthur Mossman, L.R.C.P.&S.Ed., aged 94.

No. 51

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Dec. 18.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948 (a)	1948 (b)	1948 (c)	1948 (d)	1948 (e)	1947 (Corresponding Week) (a)	1947 (b)	1947 (c)	1947 (d)	1947 (e)
Cerebrospinal fever	35	5	23	3	1	33	1	24	—	1
Deaths		—	1				1	1		
Diphtheria	124	9	36	11	5	209	19	57	11	13
Deaths	—	—	—	—	—	3	—	—	—	1
Dysentery	54	8	46	2	1	83	16	34	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	—	—	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			38	4	2			45	12	5
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				40					30	
Deaths	33	2	7	5	1	78	7	11	10	3
Measles*	9,800	180	80	60	37	3,209	133	501	139	19
Deaths†			1	—	—	2	—	—	1	—
Ophthalmia neonatorum	58	2	6	—	—	53	2	5	—	—
Deaths										
Paratyphoid fever	1	1	1 (A)	—	—	6	11	1 (B)	—	—
Deaths	—	—	1 (B) —	—	—	—	—	—	—	—
Pneumonia, influenzal	1,082	67	12	7	1	841	61	6	6	23
Deaths (from influenza)‡	24	2	—	—	—	15	2	3	2	4
Pneumonia, primary	292	67	451	37	6		50	404	24	16
Deaths				8					14	
Polio-encephalitis, acute	1	—				5	—			
Deaths							—			
Poliomyelitis, acute	28	2	2	—	—	55	4	13	4	1
Deaths§	3	1					—			
Puerperal fever		—	4		—		2	13		—
Deaths										
Puerperal pyrexia‖	95	12	7	1	—	135	16	10	—	—
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,426	64	288	173	42	2,063	159	299	44	56
Deaths†			—	—	—	1	—	2	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	7	2	1	2	—	4	—	2	5	—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	2,471	154	178	62	14	1,699	122	32	27	9
Deaths	6	—	—	—	—	10	1	1	1	—
Deaths (0–1 year) Infant mortality rate (per 1,000 live births)	325	44	52	34	10	445	48	68	37	19
Deaths (excluding still-births)	5,326	891	646	195	129	5,298	779	704	217	138
Annual death rate (per 1,000 persons living)			13·0	12·2				15·6	13·7	
Live births	7,196	1158	1011	305	219	7,858	1186	953	290	229
Annual rate per 1,000 persons living			20·4	19·1				19·2	18·3	
Stillbirths	193	23	25			201	24	28		
Rate per 1,000 total births (including stillborn)			24					29		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-epcephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* there was a decrease in the notifications of measles 294, whooping-cough 51, diphtheria 20, and dysentery 15. There were increases in the incidence of acute pneumonia 55 and scarlet fever 16.

The largest decreases in the notifications of measles were Lancashire 145, Yorkshire West Riding 126, Essex 86, and Middlesex 68; the largest increases were Durham 65 and Worcestershire 56.

The largest rises in the incidence of whooping-cough were Kent 55 and Sussex 40; the greatest fall was London 33. The chief features of the returns for diphtheria were an outbreak with 8 notifications in Yorkshire East Riding, Holderness R.D., and an increase of 8 in Essex. The largest increase in the incidence of acute pneumonia was in the south-eastern counties, where the notifications rose from 66 to 105.

The largest centres of dysentery were London 8 (Hackney 4) and Lancashire 8 (Liverpool C.B. 7). The largest return for acute poliomyelitis was Yorkshire West Riding 3.

In *Scotland* increases were recorded in the notifications of acute primary pneumonia 54 and whooping-cough 19, while a decrease of 67 was reported for measles. The rise in the incidence of pneumonia was contributed by the western area of the country.

In *Eire* there was an increase of 9 in the notifications of measles and a decrease of 12 for whooping-cough.

In *Northern Ireland* the chief feature of the returns was a decrease of 26 in the notifications of measles in Belfast C.B.

Quarterly Returns for England and Wales

During the September quarter the birth rate was 17.6 per 1,000, compared with 20.0 for the corresponding quarter of 1947. The infant mortality rate was 28 per 1,000 live births, and was the lowest rate ever recorded for any quarter and 4 below the rate for the third quarter of 1947. The stillbirth rate was 22.6 per 1,000 total births and was the lowest rate for any quarter on record. The general death rate was 9.3 per 1,000 and 0.4 above the rate for the corresponding quarter of the preceding year.

Quarterly Return for Eire

The birth rate during the September quarter was 21.9 per 1,000 and was 1.5 below the rate for the third quarter of 1947. The infant mortality rate was 38 per 1,000 registered births, and was the lowest rate yet recorded. The general death rate was 10.5, and was 0.7 below the rate for the September quarter of 1947. The death rate from the principal epidemic diseases was less than half the recent rates for the third quarters; only 125 deaths were attributed to these causes, and of these 69 were due to infantile diarrhoea and enteritis and 42 to whooping-cough. Deaths from pulmonary tuberculosis numbered 512, and deaths from other forms of tuberculosis 167; these were, respectively, 124 and 52 fewer than in the third quarter of 1947.

Week Ending December 25

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,154, whooping-cough 1,791, diphtheria 100, measles 8,959, acute pneumonia 792, cerebrospinal fever 22, acute poliomyelitis 17, dysentery 30, paratyphoid 3, and typhoid 4.

The Ministry of National Insurance states that some people may get reduced sickness and unemployment benefit from Jan. 3. These are people who were already insured when the new scheme came into operation but whose total number of contributions paid or credited for the year ended July, 1948, including arrears paid since then, was less than 50. For instance, a man with less than 26 contributions paid and credited in this period will not be entitled to benefit, but if he has more than this number the weekly rate will vary from 13s. with 26 to 29 contributions to 25s. with 48 or 49 contributions. Similar reductions will be made for dependants' benefits. Benefit may also be lost after Jan. 3 by those who have not yet handed in their 1947–8 contribution cards. Anyone who still has this card in his possession is advised to take it at once to the employment exchange and get it replaced by a National Insurance card.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Oestrogen Estimation

Q.—*What is the method of estimating oestrogen in urine, and for what purpose is it used?*

A.—Many methods have been, and still are being, used, and none can be regarded as satisfactory. Most of them consist basically in extracting the oestrogens with ether from a 24-hour specimen of urine. Thorough hydrolysis is also necessary to break up the oestrogen–glucuronic-acid combinations. The fraction containing the oestrogens is then usually assayed according to its ability to produce cornification of the vaginal epithelium in spayed female mice or rats. Colorimetric and photometric tests have also been described (Bachman, K., *J. biol. Chem.*, 1939, **131**, 455), but they are rarely employed.

It is relatively easy to demonstrate the presence of oestrogens but extremely difficult to make an accurate quantitative determination. Biological assays are notoriously unreliable, because the reactions in the test object vary with the sensitivities of individual animals of the same species, the spacing of doses, etc. Also the different excretion products (for example, oestrone, oestriol) of oestradiol have different biological activities, and the total effect depends on their relative proportions. Again, not all workers employ the same criteria for a positive biological response, and it is doubtful whether the findings of one laboratory can be compared with those of another. Apart from the technical difficulties in quantitative work, its value in clinical practice is doubtful at present. The amount of oestrogen in the urine does not necessarily reflect the blood level; indeed, it is possible that one might be high when the other is low. Moreover, oestrogen is excreted by other routes—for example, in the bile and faeces. The state of liver and renal function also affects the oestrogen content of the urine. Although quantitative estimations have been used in the hope of determining the level of ovarian and placental function, and particularly in such conditions as amenorrhoea, pregnancy toxaemia, threatened abortion, and pregnancy complicated by diabetes, such studies should still be regarded as experimental rather than of general practical application. Apart from rough qualitative tests of blood and urine, often the best practical method of estimating oestrogen production is to note the effects on the vagina and endometrium of the patient rather than on the genital tract of a test animal.

Skin Sterilization

Q.—*Is it possible to render the skin bacteriologically sterile? Is surgical spirit a reliable cleansing agent? Please comment also on the use of the following: "dettol," tincture of iodine, "cetavlon," methylated ether. Would repeated application succeed where a single application has failed?*

A.—The skin cannot be sterilized. Its "resident" flora is partly inaccessible: it is possible to destroy only the "transient" or purely superficial flora, which may include pathogens. Most of the disinfectants named, if properly applied, are capable of this, including spirit, which according to G. T. L. Archer (*British Medical Journal*, 1945, **2**, 148) is superior to ether. Tincture of iodine is perhaps the most reliable and rapidly acting; further experiments illustrating this have recently been made by Gardner (*Lancet*, 1946, **1**, 683; **2**, 760), whose work also includes observations on "dettol" and "cetavlon." These papers should be consulted for further information. If skin is prepared for operation some time beforehand, different considerations apply, and the choice may reasonably fall on a slowly acting but persistent disinfectant such as mercury perchloride or one of the antiseptic dyes or flavines. It is impossible to say which of all these procedures is the most satisfactory: no practical comparative tests on a large enough scale have ever been made, and the incidence of operation-wound infection is affected by so many other factors that any information so obtained would be of doubtful significance.

Transfusion of Infected Blood

Q.—*Is there a method of sterilizing blood from (1) potentially malarious and (2) potentially syphilitic donors?*

A.—(1) The danger of transmitting malaria occurs only when red cells are being transfused. If blood suspected of containing malaria parasites is stored for 14 days at 4° C. the majority of the plasmodia will almost certainly be destroyed or rendered non-infective. Antimalarial drugs such as quinine or mepacrine, if added to the blood, will destroy parasites, but the mixture must be kept at 37° C. for at least 24 hours, by which time some degree of haemolysis may have occurred, thus rendering the red cells unsuitable for use. Proguanil ("paludrine") has no direct action on the malarial parasites. Infections due to *Plasmodium falciparum* usually die out two years after a patient has left a malarial country; *P. vivax* and *P. malariae* may persist in the tissues for many years. If it is suspected that blood containing malaria parasites has been used for transfusion, the recipient should be placed on suppressive doses of an antimalarial drug—proguanil 100 mg. daily, or mepacrine 100 mg. daily, or chloroquine 300 mg. on one day a week. Such suppressive regimens, so long as they are continued, will usually prevent the onset of acute symptoms.

(2) *Treponema pallidum* may be transmitted in whole blood, plasma, or serum. In latent syphilis or in late tertiary syphilis it is doubtful whether spirochaetes are present in the blood stream, but in the incubation period and during the primary and secondary stages there is danger of transmitting infection by transfusion. Spirochaetes may be destroyed *in vitro* by the action of arsenicals, arsenious oxides such as "mapharsen" acting more rapidly than neoarsphenamine. H. Eagle and W. Mendelsohn (*Science*, 1938, **87**, 194) point out that the antispirochaetal action of arsenicals *in vitro* depends on a number of variables. Raising the temperature from 23° to 37° C. increases the rate of inactivation, but serum and tissue cells retard the spirochaeticidal effect. It is therefore doubtful whether this measure could be applied to whole blood. Penicillin inactivates *Treponema pallidum* in a concentration of 10,000 units per ml. when the spirochaetes are exposed for three hours at 37° C. (A. Bessemans and R. Derom, *Ann. Derm. Syph., Paris*, 1946, **6**, 744). H. Eagle (*J. Bact.*, 1946, **52**, 81) has shown that penicillin G is more active in destroying *T. pallidum* than the other forms of penicillin; the relative activities per mg. of the penicillin are: F=53, G=100, K=76, X=51. No reliable evidence is available to show how much time is required to inactivate treponemata in whole blood.

Glaucoma Simplex

Q.—*Is there anything to prevent the intense irritation of the eyes and the surrounding skin which may be due to the application of pilocarpine in oil to a patient with glaucoma simplex?*

A.—It is likely that the irritation is due to the medicament. Some patients develop these irritative symptoms after prolonged use of almost any type of drops. Oily drops are apt to be more irritating than a watery solution, and higher concentrations than lower concentrations. The patient is presumably using 0.25% pilocarpine in oil. Drops of 0.5% in watery solution three or four times a day may be better tolerated. Alternatively, eserine drops 0.25% in watery solution may also prove the better medicament. The important thing in using drops is, of course, to keep the pupil contracted and the tension under control. This, rather than tolerance to the drops, should determine whether the best procedure would not be surgical.

Fanconi's Syndrome

Q.—*What is Fanconi's syndrome, and what are the differential diagnosis and treatment?*

A.—There are two separate and distinct disorders known as Fanconi's syndrome. In chronological order these are: (1) the combination of congenital hypoplasia of the bone marrow with multiple congenital defects occurring as a familial disease (*Jb. Kinderheilk.*, 1927, **117**, 257); (2) a condition in which dysfunction of the renal tubules is associated with a hypophosphataemia, renal glycosuria, "rickets," and disturbance of amino-acid metabolism (*Jb. Kinderheilk.*, 1931, **133**, 257; *Dtsch. med. Wschr.*, 1936, **62**, 1169; *Jb. Kinderheilk.*, 1936, **147**, 299).

There is no purpose in discussing the details of differential diagnosis and treatment of these two widely different syndromes, but the questioner will find the information he requires in the papers cited.

T.A.B. in Cheiropompholyx

Q.—*What are the rationale and method of administration of T.A.B. in the treatment of cheiropompholyx?*

A.—There is no rationale for the use of T.A.B. in pompholyx; it is shock therapy and empirical. It may be given intravenously in a dosage of 100 million organisms, when a severe pyrexial reaction lasting a few days may be anticipated, or in a dosage of 10 million repeated a few times at weekly intervals, when a less severe reaction will result.

Hormone Treatment of Infertility

Q.—*Is testosterone propionate or methyl testosterone indicated, and, if so, in what dosage, for infertility in a man aged 41? His testes are abnormally small, and an examination of the seminal fluid reveals no spermatozoa. There is no other physical abnormality and no history of previous illness.*

A.—Testosterone propionate or methyl testosterone has been advocated for infertility associated with oligospermia or even azoospermia, because experimentally either maintains spermatogenesis in the hypophysectomized animal. The dosage might be in the neighbourhood of 25 mg. of the former injected three times a week, or 5 mg. of the latter thrice daily. The writer, however, has no confidence in this therapy, or even in gonadotrophin therapy, unless there is at the same time clear endocrinological evidence that the condition is secondary to a hypopituitarism. Testicular biopsy should be carried out in every case, and it is probable that in this case fibrosis and hyalinization (resulting from previous virus infection) will be found; such a condition would not respond to any hormone therapy.

Melanoma

Q.—*A man aged 57 has had from childhood a small area of black pigmentation about 5 cm. to the right and slightly below the umbilicus; it is now about 1 cm. across. The skin is freely movable and there is no proliferation of tissue. In view of the risk of malignant change, what advice should be given? Would removal provoke malignant development?*

A.—The relationship between benign and malignant melanoma is of great importance. Signs of malignant change developing are an increase in size, increase in the degree of pigmentation, the presence of moisture, and the occurrence of bleeding. When any of these signs are present in a benign melanoma it must be excised carefully. Experience proves that trauma to a benign melanoma can initiate malignant changes, and when such a tumour is subjected to constant trauma it must be excised. When excision is undertaken certain technical details are important. Excision is carried out with the scalpel; the tumour itself must not be touched by the scalpel or forceps, or traumatized in any way. The encircling incision must be placed at least 2.5 cm. from the edge of the tumour, and the underlying deep fascia is also removed over an area 4 cm. from the edge.

Secondary Syphilis

Q.—*A patient developed a secondary syphilitic rash and was treated with 14 mega units of penicillin over 14 days. She has had an intermittent course of arsenic and bismuth (0.6 g. and 2 ml. a week for three 12-week courses), but the injections upset her. Her blood was positive at the start, but she has since had three negative Wassermann reactions. Is it safe to discontinue the arsenic and bismuth when she has completed her fourth 12-week course (she has one month's rest in between courses) or should I go on for another full twelve months?*

A.—The treatment already given seems quite adequate, and as injections upset the patient further treatment might do more harm than good. It will, of course, be necessary to keep the patient under observation with periodical blood tests (say three-monthly for the first year and six-monthly for the second year) for two years after completion of treatment; the cerebrospinal fluid should be examined some time during the observation period. Should the question of pregnancy arise, careful observation throughout and perhaps a second course of penicillin would be indicated.

Enteroptosis

Q.—*Is there any recent treatment for enteroptosis? The x-ray report is as follows: "Enteroptosis and irregular spasm of lower part of colon; pelvic colon somewhat elongated; weak contractions of caecum and ascending colon."*

A.—Enteroptosis needs no treatment. A low position of the viscera is merely part of a lean asthenic habitus and there is no evidence that it is responsible for any symptoms. Exception must be made to this statement in the case of the kidney, where kinking of the ureter may occasionally give rise to a Dietl's crisis, and possibly also in the case of the spleen. For the rest "visceroptosis" is no more than the usual position assumed by the viscera in the tall thin individual. The only comment of possible significance in the radiologist's report cited by the questioner is the presence of irregular spasm in the lower part of the colon. This may result in abdominal pain, and, if it indicates the spastic colon, treatment with a low-residue diet, liquid paraffin, and antispasmodics should be of benefit.

Fluorides in Prevention of Dental Caries

Q.—*Would it be worth while for an adult who still has most of his teeth, though heavily filled, to try fluorine treatment in the hope of delaying the inevitable? If so, in what form and manner should it be used? Are there any contraindications?*

A.—The evidence that topical application of fluoride solutions is of value in halting the onset of dental caries after the eruption of the teeth is not as yet entirely convincing. In the adult, provided that regular dental attention is received, the teeth are far less likely to be lost on account of dental caries than from gingivitis. The method so far used is the topical application of 2% sodium fluoride solution to the surfaces of the teeth, after previous cleaning and drying to ensure adequate contact of the solution with the dental tissues. The optimum concentration of the solution and the number and frequency of applications are not as yet known. It must be remembered that fluoride salts are extremely toxic. The questioner should also refer to a letter on this subject published in the *Journal* of Jan. 1 at page 29.

Petit Mal

Q.—*Is anything known of the aetiology of petit mal, and is there any useful form of treatment?*

A.—Petit mal is ordinarily a constitutional affection due to a cerebral dysrhythmia, often inherited. The latest form of promising treatment consists in giving capsules of "tridione," the usual dose being 0.3 g. thrice daily. Caution is necessary owing to the risk of agranulocytosis. A subjective sensation of glare, if not photophobia, is a very common side-effect.

NOTES AND COMMENTS

Correction.—Mr. Malcolm Donaldson (chairman of the Clinical Cancer Research Committee of the British Empire Cancer Campaign) has pointed out that in our report (Dec. 18, 1948, p. 1076) of the Committee's statistical survey of cancer of the kidney, bladder, and prostate it was stated that the first symptom of the disease (cancer of the prostate) was difficult or painful micturition in 60% of cases. What the Committee actually stated was that difficult or *frequent* micturition was the first symptom in 60% of cases. Local pain in the perineum or urethra was the first symptom in only 3.7% of the cases.

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